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NERVOUS INDIGESTION

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ARTERIAL HYPERTENSION

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INTRODUCTION BY

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STALKERS OF PESTILENCE

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BY WADE W. OLIVER, M.D.

Professor of Bacteriology, Long Island College Hospital

FOREWORD BY

THEOBALD SMITH, M.D., PH.D.

Rockefeller Institute

CANCER

The Therapy of Inoperable Cancer in the Light of a Systemic Conception of Malignancy

BY WILLY MEYER, M.D.

New York

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Daily and Monthly Rhythm in the Blood Pressure of a Man With Hypertension: A Three-Year Study*

By George E. Brown, *Division of Medicine, The Mayo Clinic, Rochester, Minnesota*

In a given case of hypertension much information is desired which is not obtained by the occasional examination of the blood pressure. It is desirable to know when the blood pressure became elevated; what the factors or agents were that precipitated or accelerated the abnormal blood pressure; what the effects are of daily or hourly happenings, such as emotional upsets, the strain of daily work, worries, relaxation, vacation, changes in weather, and all the events that go to make up this highly organized, complex civilization. One would like to know the effects of intercurrent disease, and of foci of infection, on hypertension, and why in some cases the progression of the hypertension is slow and benign in its effect and in others rapid and destructive in its effect. It remains to be determined whether environmental factors enter into the production of hypertension or whether the process is due to a fixed, preordained biologic evolution for the individual person, based on the laws of inheritance.

Since these problems could not be solved from studies in the hospital or in the physician's office, the proposal of an intelligent male patient, twenty-five years of age, led to the present method of study. This patient had well defined essential hypertension, without known etiology. His father had a systolic blood pressure of 190 and a diastolic pressure of 100 millimeters of mercury. His mother's blood pressures were 124 and 78. There was no other known case of hypertension in the family. The hypertension of both the patient and his father was of the systolic type. The patient was much interested in the mechanism and pathogenesis of his hypertension and had returned to the Mayo Clinic once or twice a year for additional information on the subject. After three or four visits, he advanced the opinion that data on the subject could be secured by him taking his own readings of blood pressure and carefully studying the possible factors, each in turn, checked with adequate controls. This intelligent challenge was accepted after due consideration. He was carefully instructed in the auscultatory method of reading blood pressure, and demonstrated unusual ac-

*Submitted for publication February 17, 1930.

curacy with the method within a few days. He was an ideal subject for this type of work in that he could study the problem in a dispassionate way.

Since that time, seven additional subjects with different degrees of hypertension have been selected to carry on a similar type of study. In each instance, the question of the possible psychic effect of such study on the patient was carefully considered, and in no instance was it felt that the method was harmful. The patients in whom I was most interested were those in the early stage, before organic change had taken place. Sufficient time has not yet elapsed to allow the observations of this group as a whole to be reported. This report concerns the data obtained by one patient over a period of three years. I believe this method, properly carried out and adequately controlled, in suitable subjects, offers a means of securing information on the evolution of hypertension that cannot be obtained in any other way.

Plan of Study

The plan was to take, as a minimum, three readings of blood pressure a day, at 7 a.m., and at 6 and 10 p.m., and on some Sundays, hourly or bihourly readings. The first three months comprised the period of control. During this time the subject lived his usual unrestricted life, partook of his usual food, and indulged in his usual habits, such as late hours. In the second three months, he assumed a more restricted type of life. He ate food lower in calories than that which he usually consumed and which contained only 60 gm. of protein and a low content of salt. He assumed more regular habits of living, including a minimum of nine hours of sleep and a period of rest at midday. Every three months he consulted his physician, who verified the accuracy of his procedures and his adherence to the prescribed regimen. The effects of cold and hot weather, of high and low humidity, of variations in his daily work and of abnormal events were noted in the protocols. Once a year he returned to the Mayo Clinic for a complete study, including hourly determinations of blood pressure under activity and rest (fig. 1).

Data

In figures 2, 3 and 4 are shown the frequency distribution of morning and evening systolic pressures for the years 1926, 1927, and 1928. Careful study of these figures and of figure 5 brings out several significant points:

1. There was a seasonal lowering of the blood pressure during the summer months of each year. In August and September, 1926, there was a higher percentage incidence of values for systolic blood pressure that were in the lower range (160 to 169 mm. of mercury) than in the other months of the year. This was true of both morning and evening pressures. For 1927, the high percentage incidence of systolic pressure in this range from 160 to 169 mm. fell in July and September. This was not so striking in the evening readings. The average of the mean morning pressures, for four months including the summer, was 5.9 mm. of mercury lower than the mean morning pressures for four months, including the winter. Computed in the same way, for the same months, the evening pressures were only 1.1 mm. of mer-

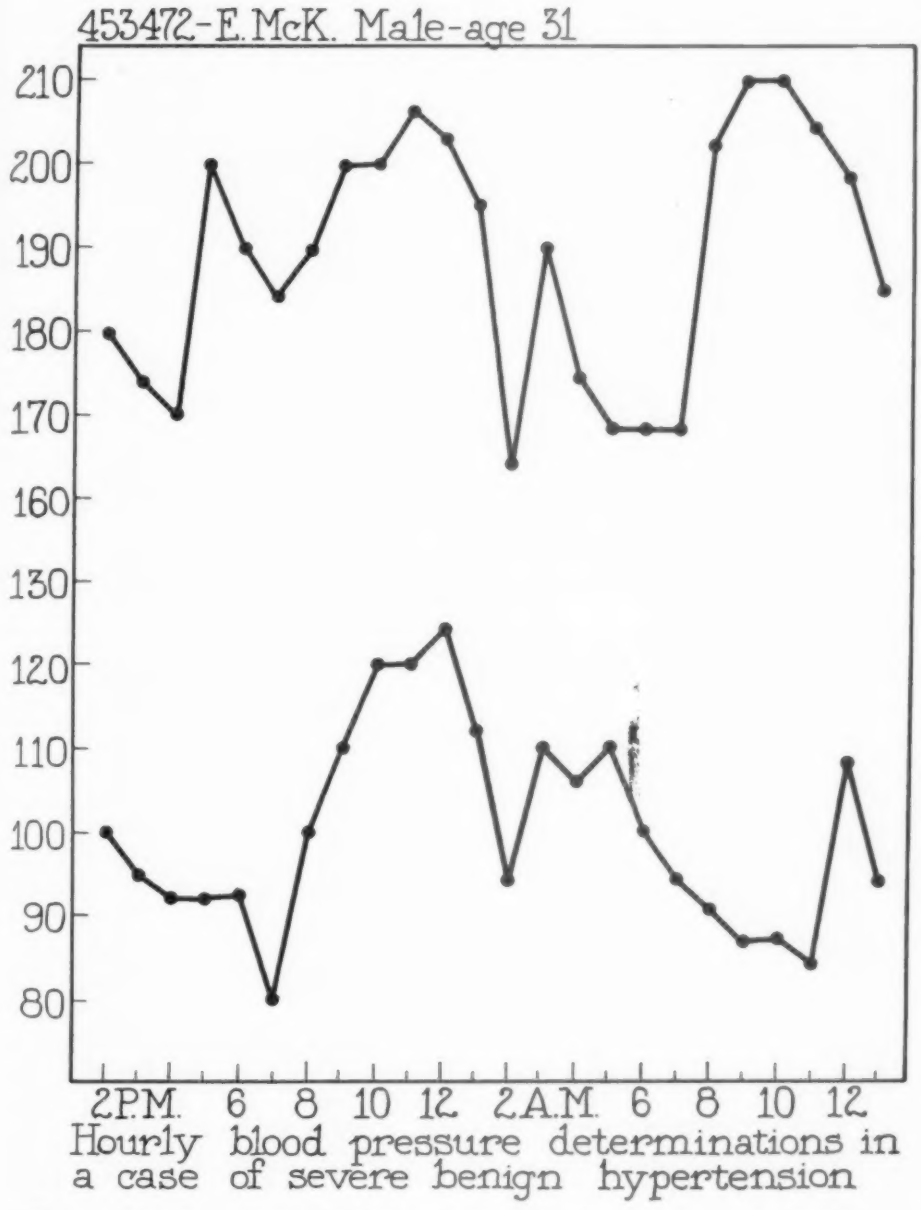

FIG. 1. Hourly readings of blood pressure while the patient was in hospital.

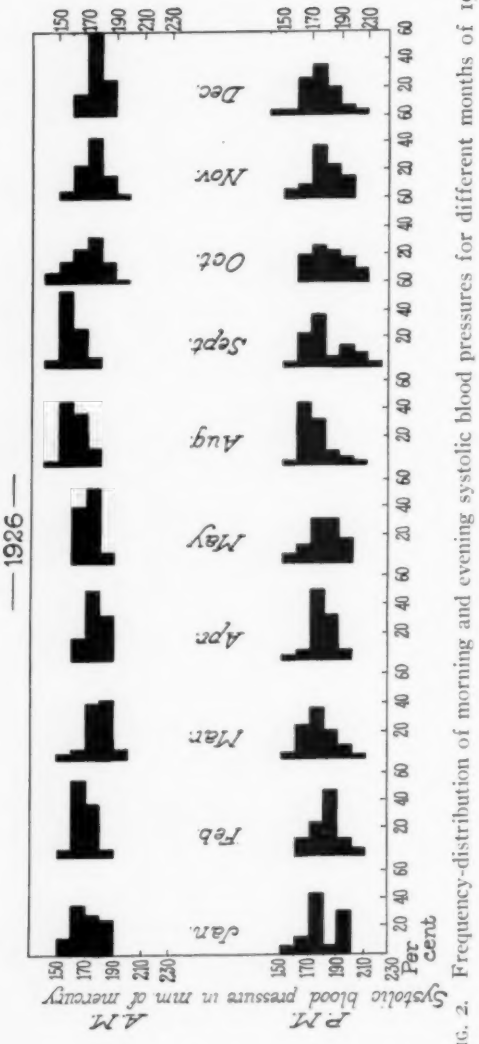

FIG. 2. Frequency-distribution of morning and evening systolic blood pressures for different months of 1926.

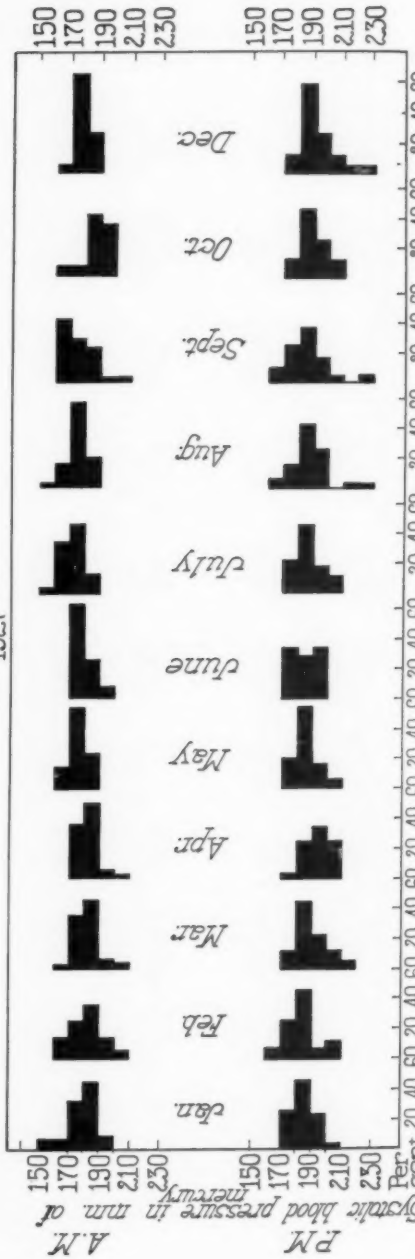

FIG. 3. Frequency-distribution of morning and evening systolic blood pressure for different months of 1927.

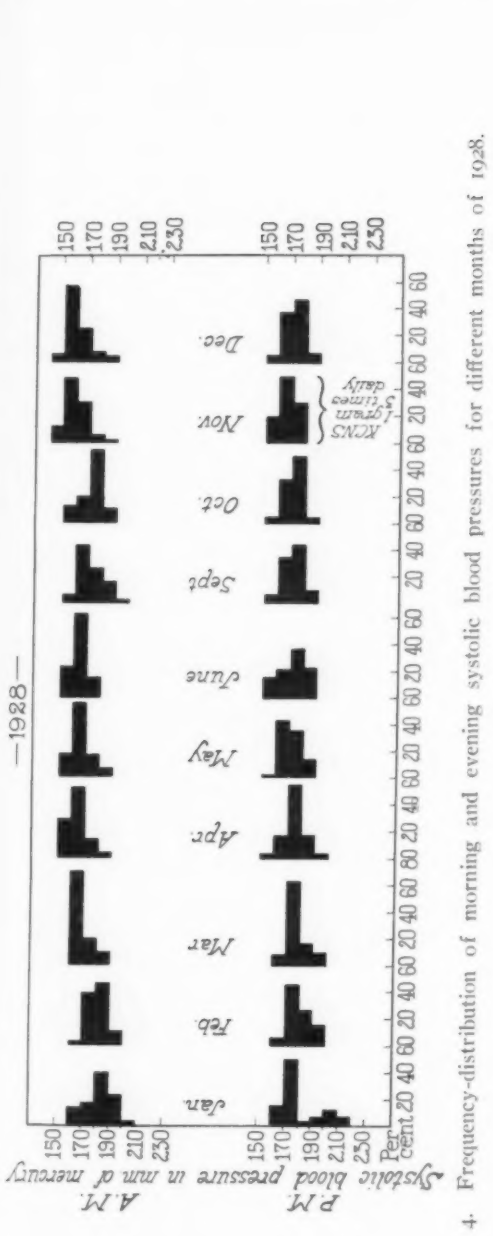

FIG. 4. Frequency-distribution of morning and evening systolic blood pressures for different months of 1928.

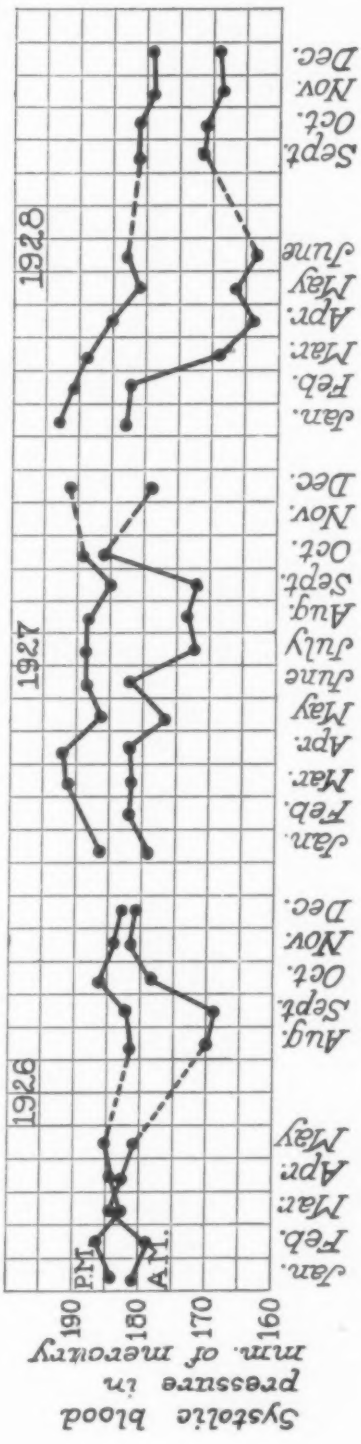
Systolic blood pressure in mm. of mercury
190 180 170 160
P.M.
A.M.
1926
1927
1928
Jan. Feb. Mar. Apr. May June July Aug. Sept. Oct. Nov. Dec.
Jan. Feb. Mar. Apr. May June Aug. Sept. Oct. Nov. Dec.
Jan. Feb. Mar. Apr. May June Sept. Oct. Nov. Dec.

FIG. 5. Mean values for morning and evening systolic blood pressures for different months of three years.

cury lower in summer. For 1928, more of the readings in March, April, May and June were in a lower range than in the rest of the year; this was less evident in the evening readings. The sharp fall in the blood pressures for these months was coincident with a change in the subject's routine of work. Previous to March, 1928, the patient retired at 9:30 p.m. and arose at 6:30 a.m.; starting in March, 1928, he retired at 12:30 a.m. and rose at 8:00 a.m. That the deviation in routine is responsible for the fall in blood pressure is probable, for in the previous years no such fall occurred in these months.

2. There was a variation in the difference between the morning and evening pressures in different months of the year. The mean values for the morning and evening systolic pressures are plotted in figure 5, for each month for three years. In 1926, for the month of March, the mean morning pressure was higher than that of the mean evening pressure. From then on, the curves of morning and of evening pressure separated, with an increasing spread between them in the months of August and September. For the balance of the year the difference was less. This curious variation in morning and evening pressures occurred also in the years following 1916, except that the morning pressures never exceeded the evening pressures. The wide separation of the morning and evening pressures during the summer months was probably of significance because it was repeated each year for the period of three years.

Blood Pressures for Days of the Week

The percentage-frequency distribution of the blood pressures for each day of the week for a period of seventeen months was studied. During this time, the patient's life was regular for the week days, and on Saturdays and Sundays he participated in the usual diversions of a young unmarried man. He attended boxing exhibitions frequently. Analysis showed approximately the same percentage frequency of morning systolic pressures of 150 to 159 mm. for each week day. However, on Sundays, Mondays and Saturdays, the frequency of pressures of 200 mm. and more was higher. The highest percentage incidence of every blood pressure below 170 mm. occurred on Tuesdays, Wednesdays, Thursdays, Fridays and Saturdays, whereas the highest percentage incidence of evening blood pressures above 200 mm. occurred on Sundays, Mondays, Thursdays and Saturdays. The mean values for the morning and for the evening systolic blood pressures for each day of the week for the three years are shown in the tabulation, and graphically in figure 6. The variation in the means of systolic and diastolic pressure showed striking differences for Sundays, as compared with other days. The mean systolic evening pressures were highest on Sundays, and gradually decreased to Tuesday; then they remained fairly constant. The mean morning pressures showed much smaller differences for the different week days. The difference between the mean morning and evening pressures was greater on Sundays; the difference gradually

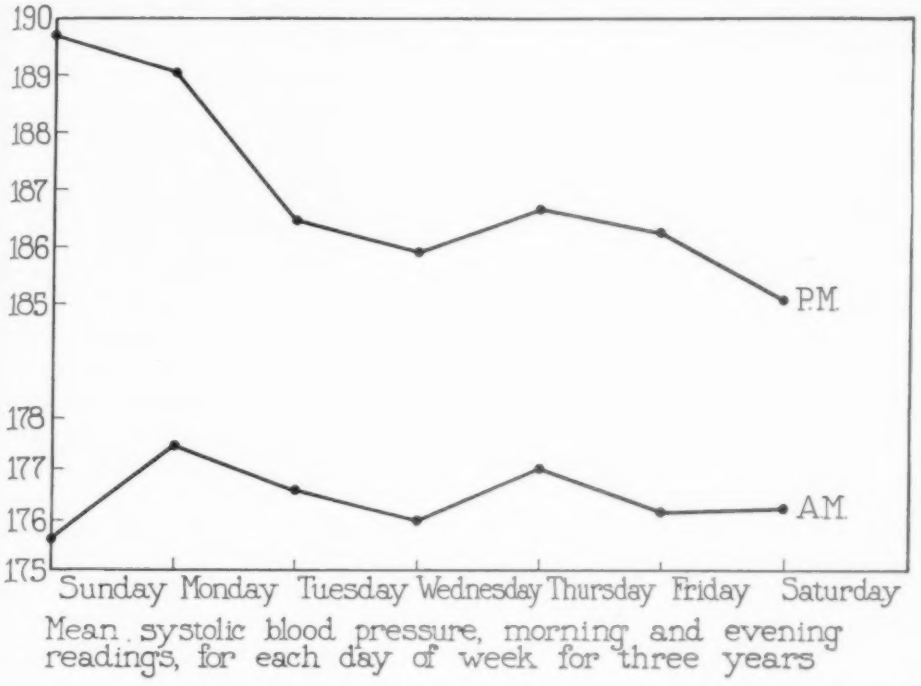

FIG. 6. Mean morning and evening systolic blood pressures for each day of the week for a period of seventeen months.

decreased to Tuesday, and from then on remained fairly constant.

The probable explanation of the variation on the different week days was offered by the patient. He noted that during the week, while he was following his regular physical labor as a steam fitter, the blood pressures tended to remain below 200 mm., and abnormally high pressures were rare; when the pressure was high during the week, it could be explained by some definite emotional upset, such as sickness of a relative or some form of excitement. On Saturdays and Sundays the usual routine became disturbed. Sunday became a day of unrest, it induced a feeling of uneasiness and irritability and these emotional reactions were reflected in the blood pressure. Also, his recreational outlets were largely associated with emotions. All forms of excitement, such as feelings of great elation and joy, were associated with a rise in the evening systolic pressure. Regular work, monotony, boredom, and depression were associated with lowered levels of blood pressure. The patient's realization of the relationship of emotion and elevated blood pressure has prompted him to attempt emotional control. By studying the responses of blood pressure to certain mental stimuli, and then practicing mental relaxation by diversion of thought, he has become convinced that these emotional pressor effects can be largely avoided.

Effects of Diet

Various diets were suggested and faithfully carried out in 1926. The first three months of this year no modification was made in his diet. With this period as a control, during the subsequent months diets low in protein, low in calories and low in salt were instituted, without any significant change in blood pressure. It was thought, at first, that the lowering of pressure which occurred in August may have been related to the effect of diet, but the repetition of the summer drop in blood pressure in subsequent years, without dietary restriction, settled this point. The patient's impression was that effects of diet were not demonstrable.

Effects of Drugs

Two drugs were given; phenobarbital and potassium sulphocyanate. The former was given in doses of ¾ grain (0.05 gm.) once, twice and three times daily. During the period of administration, no significant lowering of the mean blood pressure nor significant changes in the percentage-frequencies of the various groups, made up on the basis of intervals of 10 mm. of pressure, were evident. Administration of potassium sulphocyanate was instituted in November, 1928, and the drug was given in doses of 1½ grains (0.1 gm.) twice daily for the entire month. There was slight resultant lowering of the morning systolic pressure; that is, the mean value for morning systolic pressure was lower than the corresponding value for November, 1926, or for the preceding month. The effect on the mean evening pressure was slightly less, and was so little that it was not significant. The polygons illustrating frequency distribution for eight months are shown in figure 7. Next, potassium sulphocyanate was given for four months in dosages of 1½ grains (0.1 gm.) three times a day. The percentage of morning systolic blood pressures that were below 170 mm. increased in February, March and April. The effects of the drugs on the evening systolic pressures were less decisive but the majority of readings of blood pressure were in the range of 180 to 189 mm. The spread of blood pressure readings was restricted. The effect of potassium sulphocyanate on the blood pressure was apparently cumulative. The blood pressures were lower for the second month of administration than for the first month. In figure 8 are shown the mean morning and evening systolic pressures for each of the eight months on which figure 7 is based. There is a curious separation of the curves of these morning and evening pressures in January, February, March and April, during which time potassium sulphocyanate was given, and there was steady lowering of the mean systolic morning pressure and consistent elevation of the mean evening pressure.

Comment

The information obtained by this method of study of the blood pressure seems significant. It is true that the method has a limited application and is applicable only to certain types of patients. A sufficient number of years has not elapsed to give an adequate picture of the course and evolution of the hypertension in this patient, but certain facts are becoming clear. The

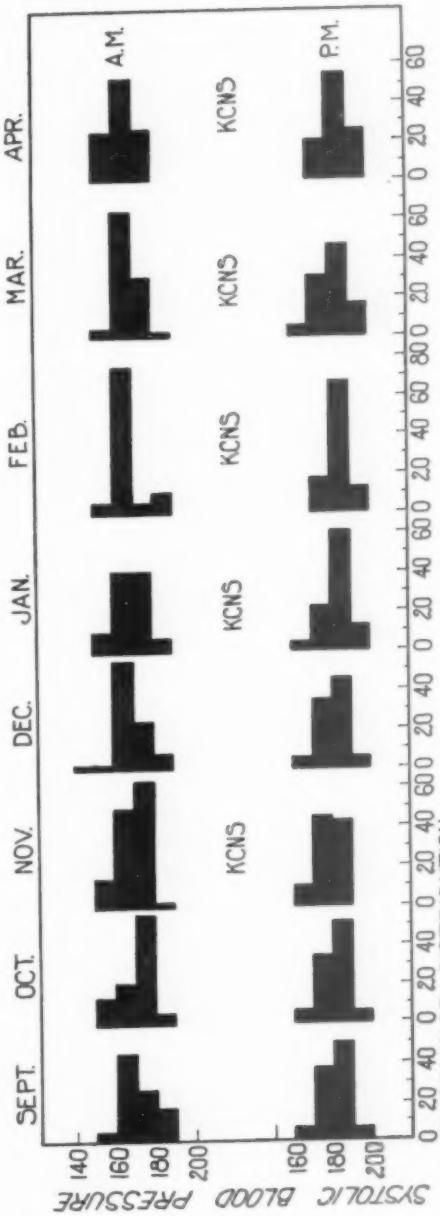

FIG. 7. Frequency distribution of the morning and evening systolic blood pressures during administration of postassium sulphocyanate.

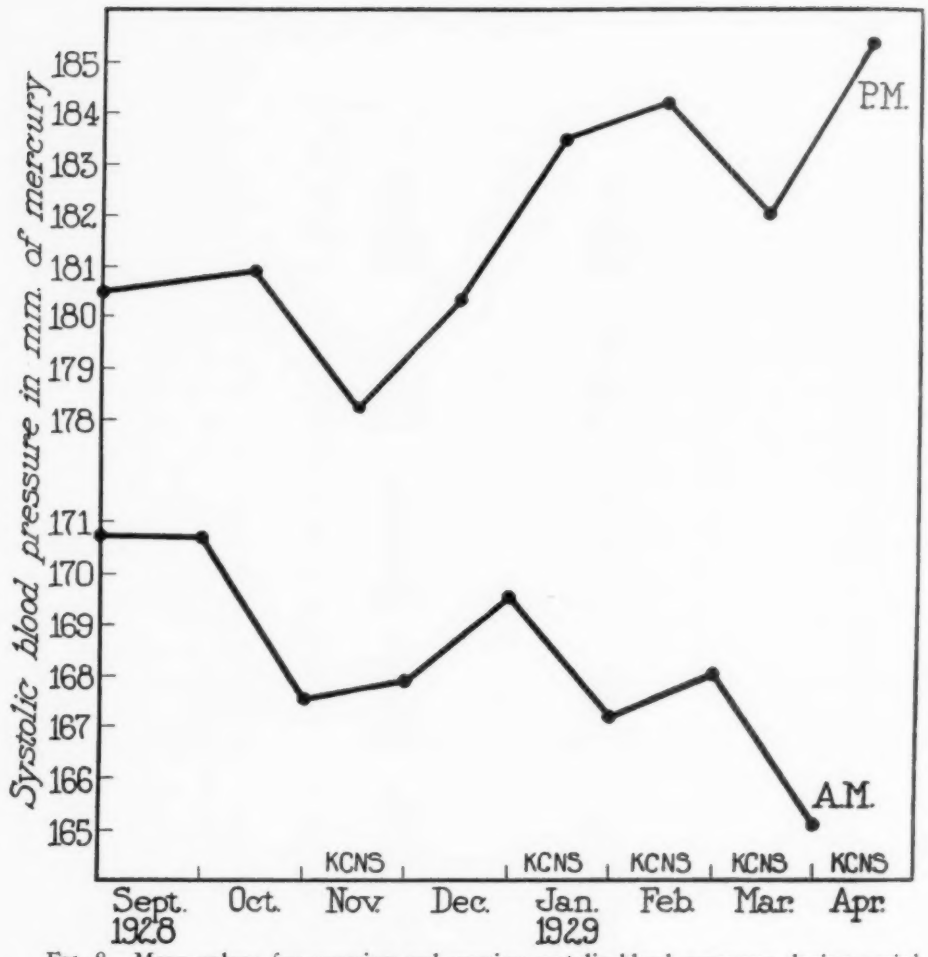

FIG. 8. Mean values for morning and evening systolic blood pressures during period of administration of potassium sulphocyanate.

most significant of these is the seasonal lowering of the systolic blood pressure. Such a lowering in warm weather has been noted by others and is ascribed to the vasomotor effects of warm environmental temperatures. The studies of McCay and Cadbury indicate definitely lower average blood pressures in persons of Oriental races as compared with inhabitants of North America. Albutt showed that there is a lower blood pressure in the brachial arteries during hot weather. The seasonal variation may not be due entirely to temperature, but other factors may play a part. There may be a relationship to ultraviolet radiation and to barometric pressures. These factors should be studied in relation to blood pressure. The separation between the curves of morning and evening systolic pressures in the late spring and summer months is of interest. This is in accord with the observation that the

depressor effect of hot weather is exerted more markedly on the morning pressures. These observations on the probable effects of season on the vasomotor mechanism seem to have a practical application in the handling of cases of hypertension. Winter migrations from northern latitudes to warmer climates, when possible, might constitute the most effective protective measure that could be used to influence blood pressure. This is borne out also by the known high incidence of patients with cardiorenal-vascular disease in the colder months. Intercurrent infection and vasomotor pressor effects, or both, may play an important part in the high death rate.

This method of study is of great value in determining the effects of therapeutic agents. It affords data for use as a control and this allows fairly conclusive deductions to be drawn. If this form of control is lacking, any statement concerning the effect of treatment on the blood pressure is impaired. I am convinced, from the data obtained in study of this patient, that potassium sulphocyanate had an effect on his blood pressure. Potassium sulphocyanate, when given fairly continuously in doses of 1½ grains (0.1 gm.) two or three times a day, produces lowering of the mean morning systolic blood pressure. Its effect is evident after the drug has been given at least a month. There is separation of the curves of mean morning and evening pressures during the winter months of administration, which is not seasonal. The morning pressure is lowered, as the effect of the potassium sulphocyanate, but, what is more significant, the blood pressures are stabilized. The range of variation of both morning and evening blood pressures is more restricted than when the drug is not given. This suggests that perhaps the usefulness of this drug will be confined to subjects with hypertension with marked variation in pressure. Its effect may be beneficial through a steadying effect on the vasomotor mechanism. I am of the opinion that this section may be significant from the standpoint of diminishing vascular wear and tear more than from the standpoint of simple lowering of the blood pressure.

This study enforces the already existing knowledge of the significance of emotion on blood pressure, and emphasizes the need for training of the emotions of certain persons with the variable, fluctuating forms of hypertension. This method should have a broader application in the attempt to secure knowledge on the subject of hypertension. I would advance the opinion that if funds for research were used for subsidizing selected subjects with familial tendencies to cardiovascular disease and the investigation were carried out over a period of years, more information concerning certain phases of the difficult problem of hypertension would be obtained than would be produced by research restricted to a less clinical type of investigation.

Summary

Determination of the blood pressure three times daily has been carried out by a patient with essential hypertension, over a period of three years.

There is greater separation of the curves of morning and evening systolic blood pressures in the summer months.

OBSERVATIONS OF MEAN BLOOD PRESSURE DURING THE COURSE OF THREE YEARS

	Sunday		Monday		Tuesday		Wednesday		Thursday		Friday		Saturday	
	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.	a.m.	p.m.
Observations	107	112	104	114	116	114	117	118	115	115	115	113	112	113
Mean value	175.6	189.5	177.5	188.7	176.6	184.8	176.0	185.2	177.1	186.0	176.2	185.6	176.3	184.3
Probable error of mean	0.8	0.7	0.7	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.8	0.7	0.7
Standard deviation of distribution	12.6	11.0	10.0	10.0	10.5	11.0	11.0	9.7	11.7	11.7	10.7	12.0	10.5	10.4

The morning and evening pressures tend to approach each other in the spring and in the autumn.

Mean systolic blood pressures for each day of the week, during a period of three years, indicate an increase in the systolic pressure on Sunday evening. It gradually becomes lower during the week.

Potassium sulphocyanate, when given over periods of months, has a lowering effect on the mean morning systolic blood pressure, and tends to cause the readings of blood pressure to fall within a small range. This suggests that this drug exerts a sedative or stabilizing effect on the vasomotor mechanism.

Further investigations of this type, carried out by intelligent patients, offer an excellent method for study of certain phases of hypertension.

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Hourly Rhythms in Blood Pressure in Persons With Normal and Elevated Pressures*

By Selma C. Mueller, M.D., *Fellow in Medicine, The Mayo Foundation,* and George E. Brown, M.D., *Division of Medicine, The Mayo Clinic, Rochester, Minnesota*

It has been known that the systemic blood pressure is not fixed, but is subject to variations from moment to moment and from hour to hour. Many workers have called attention to this variability of the blood pressure, particularly in certain forms of essential hypertension. It, however, has not been demonstrated whether there is any constant rhythm or variation in vasomotor activity in the curve of twenty-four hours. Studies have been carried out, notably by Campbell and Blankenhorn, in which, during sleep, there has been demonstrated a gradual fall in vasomotor activity succeeded by a rise in the early morning hours. It seems to us probable that there should be rhythmic changes in vasomotor behavior in human beings, related to periods of activity and rest.

With the idea of determining the existence or nonexistence of a periodic rhythm of systolic and diastolic blood pressures in twenty-four hours, the following plan has been carried out: Blood pressures have been taken hourly, for twenty-four hours, under fairly uniform conditions of hospitalization, in which environmental control was probably as constant as could be obtained. These studies were made on subjects with normal, with subnormal, and with high blood pressures. In addition to the investigation of vasomotor rhythm, certain other observations were made: The range of variability of blood pressure from hour to hour was studied; an attempt was made to demonstrate the relationship of the mean systolic blood pressure to the degree of this variability and it was hoped to determine whether different diseases distort or eliminate the normal rhythm.

Method of Study

Sixty-one patients with essential hypertension, who were in the hospital, were employed as subjects and hourly determinations of blood pressure were made over a period of twenty-four hours. Unless symptoms such as severe headache contraindicated activity, the patients were told to walk about the hospital and to simulate, to a degree, their normal activity. It was explained to them that the blood pressure would be taken every hour for the twenty-four hours and that they were to try to obtain as much sleep as possible in spite of the hourly disturbance at night. In the majority of cases, the

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patients were somewhat discomposed by the taking of blood pressure during the sleeping hours; others did not waken. The more excitable and nervous persons were more perturbed than others by this procedure and the readings of blood pressure reflected their reaction in a striking way.

All readings were made with mercury sphygmomanometers by student nurses. These young women had been trained in the taking of blood pressures with this apparatus by the auscultatory method, and their determinations frequently were verified by physicians and by use of the Tycos self-registering sphygmomanometer. The readings were immediately charted on blanks prepared for this purpose, so that the result at the end of the period of twenty-four hours was a continuous curve, as shown in figures 1 and 2.

For a control study, twenty-six similar records were made of ambulatory patients, on the various medical services, who did not have hypertension. Patients with fever or with evidence of exhausting illness were not included; many had mild grades of chronic infectious arthritis, thromboangiitis obliterans and chronic nervous exhaustion. Obviously these control

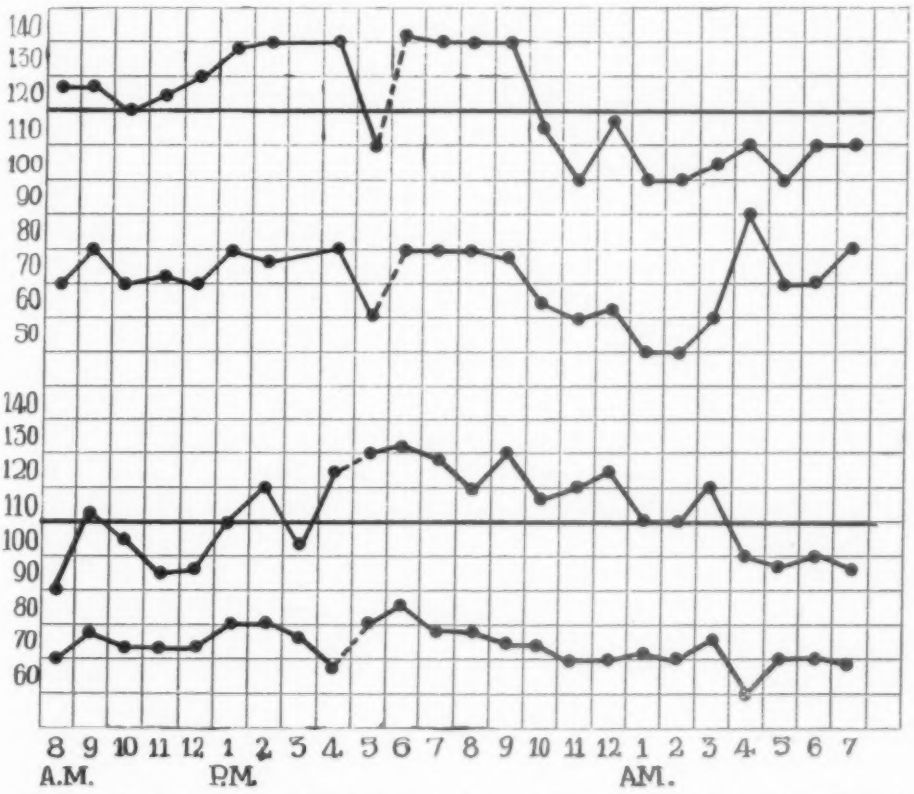

FIG. 1. Typical curves of blood-pressure of two patients in the control series. Records were taken every hour for twenty-four hours. In each instance the upper of the two curves represents the systolic pressure.

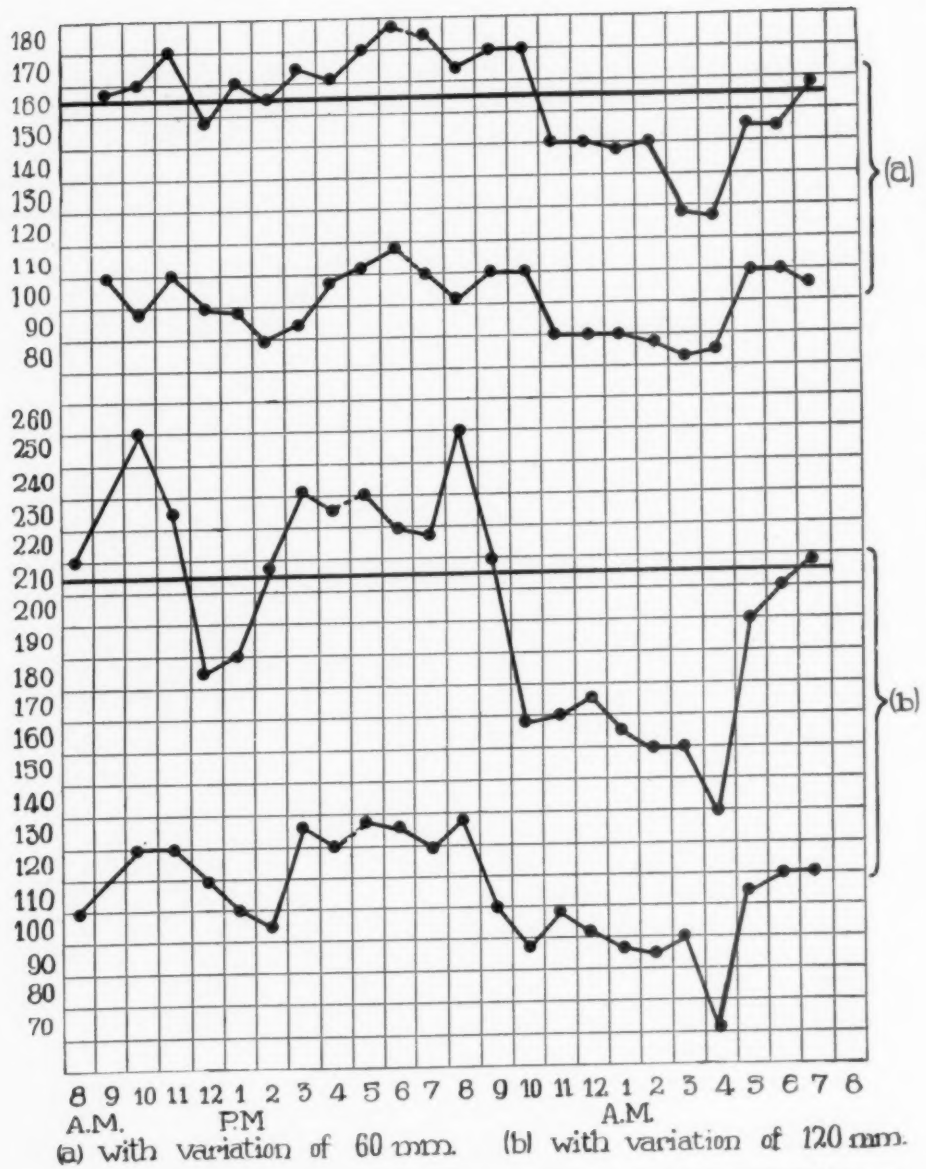

FIG. 2. Typical curves of blood pressure in cases of essential hypertension: *a*, a patient with moderate fluctuations; *b*, a patient with marked fluctuations. In each instance the upper of the two curves represents the systolic pressure.

patients were not in every way normal, but at least they had pressures less than 140 mm. of mercury. Figure 1 illustrates two normal curves.

Statistical Treatment

In order to obtain some idea of central tendency, the median, or mid-value was determined in each series of readings made in the twenty-four hours in each of the two groups. The median was taken rather than the mean because, when there are few data and some of them are widely divergent, the median gives a better idea of central tendency. In the illustrations the hourly readings of blood pressure have been expressed as the plus or minus deviation in millimeters of mercury from the median value.

Data in the Group of Controls

The fluctuations which occurred in blood pressure in twenty-four hours are shown in figure 1. In the group of controls, the greatest variation in systolic pressure in twenty-four hours was 65 mm. of mercury, the least, 15 mm. of mercury, and the average, 36.5 mm. of mercury. The highest median pressure of any subject in the group was 125 mm., the lowest, 90 mm., and the mean of the twenty-six median pressures was 107.5 mm., which is lower than the average systolic pressure for normal persons, given by Norris. Two of these patients had one reading, each, of 155 mm. and 145 mm., but since their median pressures were 115 and 105, respectively, the records were not discarded. The diastolic pressures corresponding to these systolic readings did not exceed 90 mm. of mercury.

Figure 3 illustrates in the control cases the consecutive readings throughout twenty-four hours. If one can imagine all the curves for median pressure superimposed one on the other, and each actual reading designated as five or twenty points above or below its median, as the case may be, this picture results. It will be seen that there is a tendency for the pressures to rise in the late afternoon and early evening hours. After this they gradually drop, reaching their minimum at 4 a. m., and again they rise to the morning level. Out of a total of 591 readings of blood pressure included in this group, thirty-three were 20 mm. or more above the median pressures, whereas eighteen of the readings were 20 mm. or more below the median. As is shown in figure 1, the curve of the diastolic readings was similar to that of the systolic readings, but with somewhat smaller hourly fluctuations.

The significance of the changes in level in the curves following meals will be considered later.

Data in Cases of Hypertension

Sixty-one records of pressures studied for twenty-four hours, with an occasional hourly reading missed, have been included in this group. Many more patients were studied, but some of the records were so incomplete that they were discarded. Figure 2 illustrates two typical records: one shows moderate fluctuation; the other marked fluctuations. All readings were again expressed in terms of millimeters above or below the median, and the curves superimposed, as shown in figure 4. This brings out the fact that in cases of hypertension there was a gradual

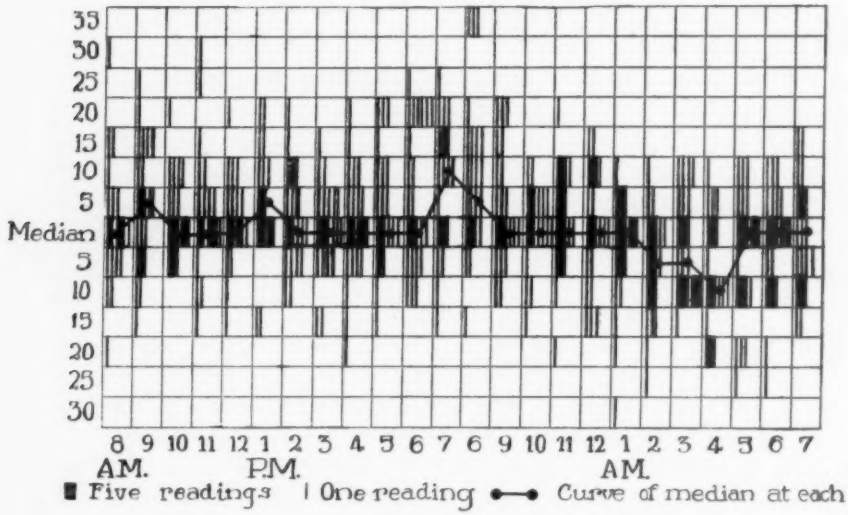

FIG. 3. Variations from the median curve of systolic blood pressure in twenty-six subjects used as controls. Records were made each hour for twenty-four hours. Heavy black lines represent five readings; light black lines represent single readings.

rise of blood pressure during the late afternoon and early evening hours; then, a gradual fall beginning in the evening and reaching its minimal point at 3 a. m. From then on there was a rise to the morning level.

There were, as previously, many readings which varied widely from the median. In about a third of these records there was a drop below the median soon after dinner; in a third, there was no drop in the early morning hours.

Figure 5 shows the daily curve for a group of eighteen patients selected from the sixty-one who were studied. These eighteen had hypertension of the labile type, with total daily variations in pressure of 70 mm. or more. The greatest variation was 120 mm. Except for the fact that fluctuations were greater than in the other groups, they were no different, and they followed the same hourly rhythm.

In practically all cases the diastolic readings varied with the systolic, as may be seen in figure 2, but usually the excursions of the diastolic pressure were smaller; actually they were from 0 to 50 mm. less than the total systolic variations. In only seven cases of the entire series was the total diastolic variation 5 to 10 mm. greater than the systolic.

In this series of sixty-one curves, based on hourly records, with a total of 1,411 readings, 165 readings (11.6 per cent) were 20 mm. or more above the median, whereas another 165 were 20 mm. or more below the median. Twenty millimeters was chosen arbitrarily as a standard, since 40 mm. was about the average diurnal variation in the control group. Thus the percentage of readings varying 40 mm. or more from their medians was three times greater in this group than in the control group. In the group of

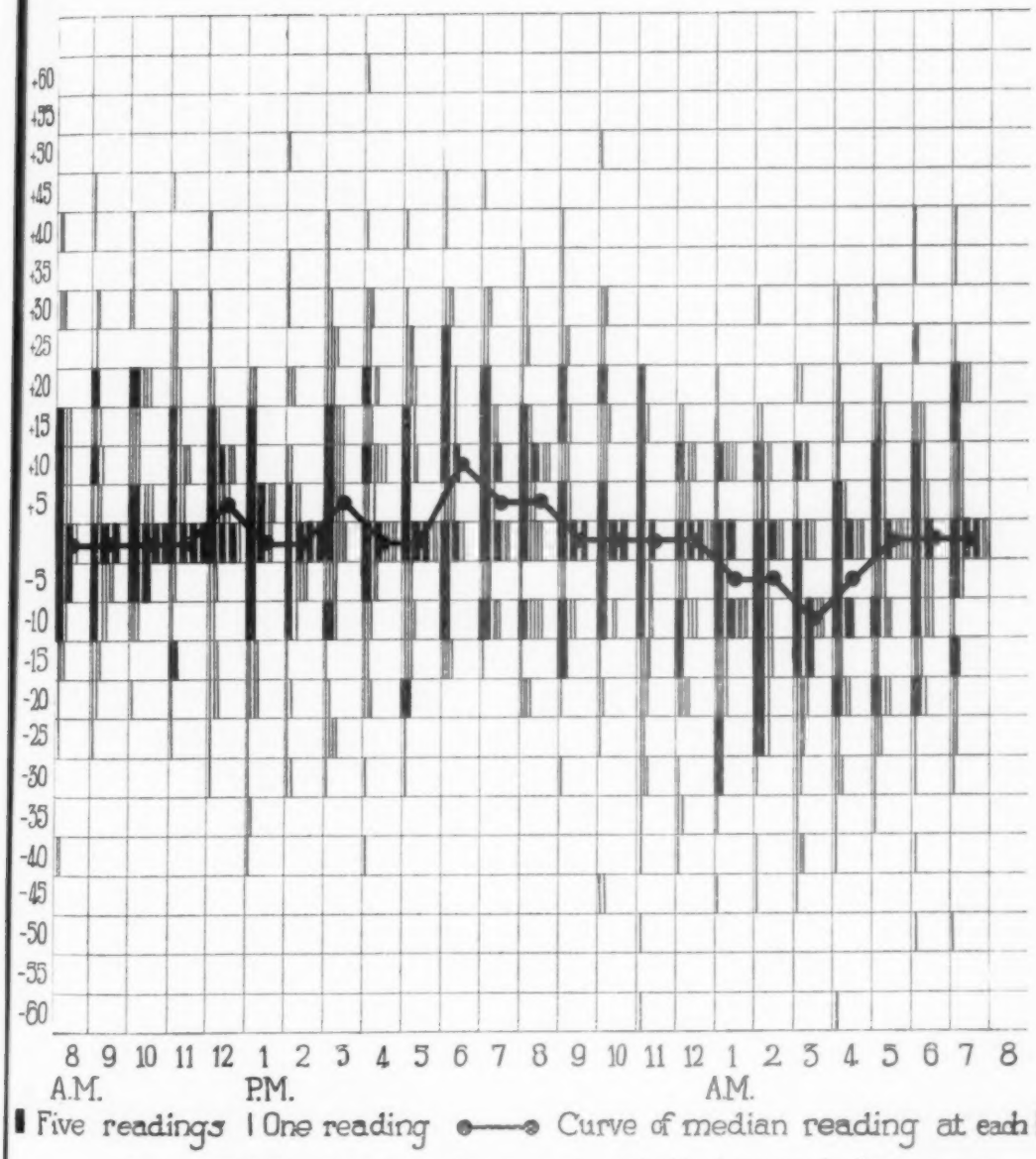

FIG. 4. Variations from the median curve of systolic blood pressure in sixty-one cases of essential hypertension. Records were made each hour for twenty-four hours. Heavy black lines represent five readings; light black lines represent single readings.

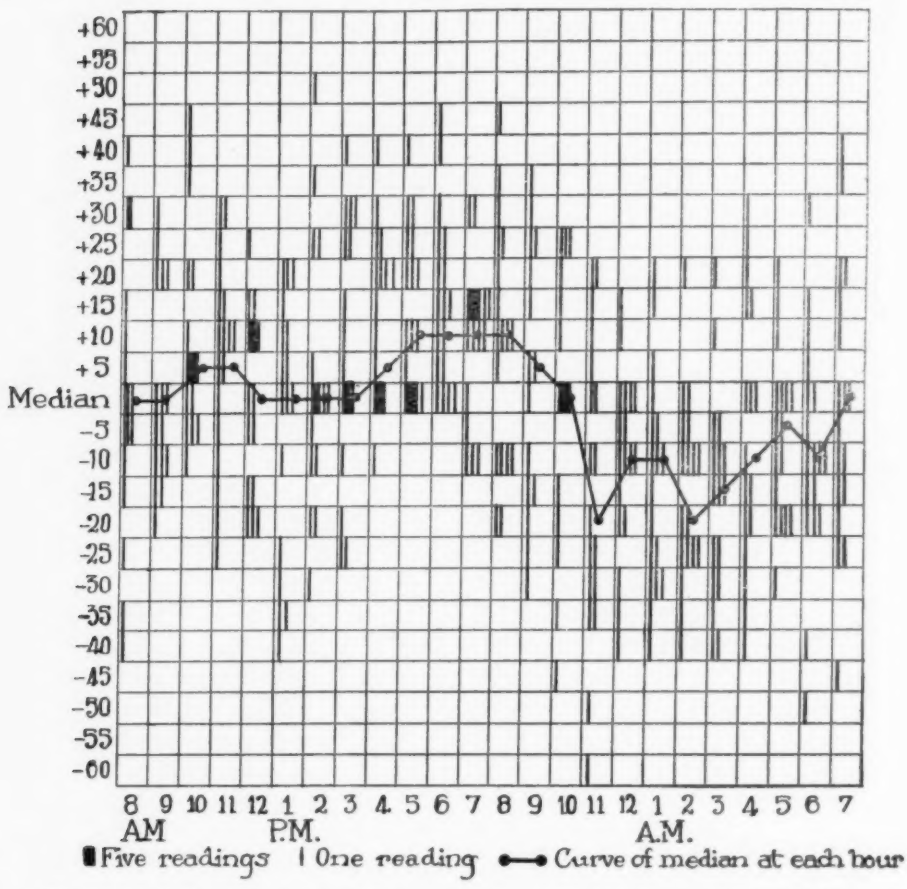

FIG. 5. Variations from the median curve of systolic blood pressure in eighteen cases of essential hypertension in which fluctuations were marked. Records were made each hour for twenty-four hours. Heavy black lines represent five readings; light black lines represent single readings.

patients with hypertension, the greatest systolic variation in the twenty-four hours was 120 mm.; the least, 25 mm. The mean daily variation of all cases with hypertension was 55 mm. The composite chart of the data concerning patients with hypertension disclosed the same rhythm in variation which was found in the controls. The only difference was that the amplitude of the upward and downward swings in the curves was greater.

COMMENT

It has long been known that in the experimental animal there are spontaneous variations in blood pressure as well as variations of the cardiac, respiratory, and Traube-Hering types. In man, Sigler has shown, in periods of ten to twenty-five minutes, that in the majority of a group of patients with normal blood pressure and who are at rest, there are no variations in pressure of more than 30 mm. of mer-

cury. In the hypertensive group all showed variations of 40 mm. or more. All investigators who have studied blood pressure during sleep are agreed that there is a considerabl : drop during the first two hours. Colombo, in 1899, was one of the first to show this, and he published records of blood pressure taken at hourly and half-hourly periods during the twenty-four hours. He emphasized the drop in pressure during sleep. Among others, Brush and Fayerweather, Janeway, Brooks and Carroll, and Campbell and Blankenhorn emphasized the drop during sleep. Campbell and Blankenhorn concluded that the fall during sleep in patients with hypertension was, in general, less than that in normal persons; in some cases of hypertension there was no fall during sleep. Our data do not confirm this for the entire group of hypertensive subjects, but in certain persons with fixed levels of hypertension there was no signficant fall in pressure during sleep. Brooks and Carroll made the observation that in persons who slept at night the fall in pressure occurred during the night, whereas in persons who slept in the daytime the blood pressure fell to its lowest levels during the day. This is to be expected if sleep is considered the essential factor in the drop. MacWilliams, in 1923, emphasized the variations which may occur even during sleep. These are to be explained, he said, by dreams and nightmares, and he thought the same explanation held for the frequent occurrence at night of cerebral hemorrhages and anginal attacks.

A number of observers have found a rise in blood pressure after meals. By no means all of our records indicated a rise after meals, although such a rise was present in a large enough number to make it evident in the median value. In the control group, there was a rise of 5 mm. in the median value at 9 a.m. and at 1 p.m., which are hours following meals. At 7 p.m., in this group, there was an average rise of 10 mm. In the patients with hypertension, however (fig. 4), the peaks in the median value occurred at 12 noon, 3 p.m. and 6 p.m. At 3 p.m., three hours after the noon-day meal, there was a rise in the median value which could not be related to the preceding meal but which might be due to the mild excitement of the visiting hour. At 7 p.m. the greatest number of rises occurred and reached their maximal height at 8 p.m. This was the culmination of the gradual rise in the later afternoon and early evening hours which was shown in the majority of the individual curves. There was a gradual fall, reaching the minimum at 3 a.m., in the patients with hypertension, and at 4 a. m. in the control patients. The pressure rose again to the time of waking. Erlanger and Hooker stated that they believed diurnal variations could be explained by the effect of the ingestion of food, and that the gradual rise during the day might be explained in this way. Our studies do not confirm this view because increase in pressures occurred during times of the day remote from meals. Colombo showed a drop in pressure following meals, which lasted for four hours; the maximal drop was 20 mm. He attributed this drop to great dilatation of the abdominal visceral vessels, and believed that variations in the

tonus of the vessels of the extremities played little part in regulating blood pressure. That the gradual rise in blood pressure during the day might be a phenomenon of fatigue has been considered. It may be due to gradually increasing tonus of the walls of the vessels, or to a cumulative effect of nonsubjective fatigue. This gradually rising blood pressure during the day is most constant and is present in subjects with normal blood pressures as well as in those in whom the blood pressures are elevated. Erlanger and Hooker brought this out in their studies in 1904, and Kylin emphasized this observation.

The drop in blood pressure during sleep may be explained by mental and physical rest, a diminished rate of circulation, with relaxation of sympathetic tonus in the arterioles. Landis, however, brought up the question whether the circulatory changes are the cause or the result of sleep. A drop in blood pressure can be effected through physical rest, but mental relaxation usually occurs at the same time. This would seem to point to the fact that mere mental relaxation, although not as complete as in sleep, nevertheless plays a part in lowering of blood pressure, just as mental stimulation causes a marked rise in pressure. The reclining posture is probably important, since in some patients with insomnia there is reduction in pressure at night. Brooks and Carroll, and others, are of the opinion that mental and psychic rest determine, in large degree, the benefit derived from rest in cases of high blood pressure. They made the observation that the drop in pressure after the regular sleep of the night is greater than after sleep taken at irregular intervals.

The great and sudden fluctuations noted in some our records of patients with hypertension were in many instances due to known psychic stimuli, such as that produced by visitors, by the physician entering the room, and so forth. These sudden marked changes are some of the most interesting observations resulting from our studies. In general, it may be said that the patient with hypertension shows extreme reactions to stimuli which in the normal person would cause only mild reactions. This is in accordance with the view of Norris, who said that hypertension is an exaggeration of a normal physiologic process, in which the whole vasomotor mechanism is sensitized. Kylin stated that the characteristic of essential hypertension is not so much the increased pressure as the extreme lability of the pressure. O'Hare stressed the same points. Sigler concluded, as have others, that the changes in blood pressure are dependent on instability of the vegetative nervous system. In a recent article, Sigler explained variations in blood pressure as being due to changes in the blood supply of the vasomotor center in the medulla. It has been shown experimentally that diminished blood supply to the medulla causes a rise of blood pressure. This rise, according to Sigler, improves the blood supply to the medulla, thus causing a drop in pressure, and a cycle of events occurs which may account for the sudden and extreme variation in blood pressure.

This study of rhythm in blood pressure in twenty-four hours constitutes

an interesting and effective study of sympathetic tonus. It confirms much preceding work and demonstrates the rise and fall of blood pressure during the active period of the day and during the resting period during the night. We are not convinced that activity, physical or mental, is the sole explanation. A series of cases have been studied during periods of complete rest for twenty-four hours. The same biphasic wave in blood pressure occurs, but is less marked. Of course, during waking hours, mental activity is present in some degree. It seems that the sympathetic nervous system of the hypertensive person responds in the same manner, only in an exaggerated degree, as does that of the subject with normal blood pressure; the same vasomotor rhythm occurs, but is less marked than in those with normal blood pressures. To the patient with hypertension, the cost of work or the cost of activity, as expressed in millimeters of mercury, is excessive. This is especially true of those who have the disease in its early form or in the stage before organic changes have taken place. This cost of effort, as measured in variations in blood pressure, is borne by the heart and arteries and seems an adequate explanation of the premature ageing of these tissues in cases of hypertension.

Summary and Conclusions

Studies of blood pressure at hourly intervals during the day and night have been carried out under controlled conditions in the hospital on twenty-six subjects with normal or subnormal systolic blood pressures and on sixty-one subjects with varying grades of hypertension.

Rhythmic changes in the level of pressure have been observed. There is a gradual rise during the day, and a fall during the night. The maximal rise is expressed in the median at 6 or 7 p.m. and the minimal drop is attained at 3 to 4 a.m.; from then on there is a gradual rise to the level of the morning.

In both groups there are three peaks which seem related to meals. In the group with hypertension there is a peak at 3 p.m. which may be related to the visiting hour at the hospital. The maximal peak occurs between 6 and 7 p.m.

There is a relation between the height of the mean systolic pressure and the amount of variability of the hourly blood pressure.

These studies support the view that the activity of the sympathetic nervous system in hypertension is not abnormal in type, but only in degree. There is simply an exaggeration of the normal response.

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Defective Liver Function As a Cause of Chronic Endogenous Skin Lesions*

By Frank Smithies, M.D., Sc.D., *Chicago*

In the course of general medical practice, during the past nine years, there has come under my observation a group of patients affected with digestive disorders and chronic skin lesions. In all patients, the dermatoses were of long duration and, in spite of most skillful care by specialists, had become unsightly, and, not rarely, deforming. Frequently enough, the skin lesions were as distressing to the patients as were their dyspeptic upsets.

From the digestive standpoint, the disturbance was of the type colloquially styled "biliousness," manifested either constantly or at intervals. In character, the clinical or pathologic aspects of these ailments satisfied our conception of chronic cholecystodochitis with or without calculi, and of chronic hepatitis. Specifically, my attention was rather dramatically attracted to the possible relationship between certain dermatoses and deficient hepatic function by a patient, the main features of whose clinical course were as follows:

A middle aged woman, of good general nourishment, wife of an Illinois physician, had been for many years a "bilious" dyspeptic. Approximately three years before the patient was seen by me, a cholecystectomy was performed at a well known clinic. A month following cholecystectomy, a Chicago surgeon performed a second operation for sub-hepatic abscess. The patient recovered from the surgical traumata very well but within a few months had return of a dyspepsia of precisely the same type as she had experienced before operation. Shortly after this recrudescence, typical lesions of psoriasis developed at the elbows, thighs, knees and neck. The skin lesions became chronic; exacerbations constantly appeared shortly following bilious attacks of unusual severity. Local applications to the skin, special forms of diet, vaccines and particular attention to general hygiene decreased neither the "biliousness" nor the psoriasis. The patient's husband brought her for general examination and, if possible, for relief from the digestive upset; the dermatosis was considered incurable: the patient and her family had become reconciled to

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the condition. The results of the examination are summarized below.

Case 3091—*Mrs. Dr. McI.* Age 46.

Past "Bilious" attacks since childhood; intense *jaundice* 15 yrs. ago. Operative history: Partial hysterectomy (Murphy, 1914); cholecystectomy (W. J. Mayo, June, 1917); stab drainage July 17, 1917 (C. D. Webster).

Complaint—Well for several months after gall bladder operations, then had *right costal pain, jaundice, clay-colored stools*; surgeons again consulted but she was not re-operated; diet advised; icterus slowly disappeared; but dyspepsia practically constant.

At present, headaches, dizziness, hepatic region pain, nausea, irregular type dyspepsia.

Physical examination—liver enlarged 3-½ cm.; tenderness over common duct zone; head of pancreas swollen, tender, palpable; extensive psoriasis; moderate undernourishment.

Laboratory—Stomach, Free HCl 29; T.A. 74; no retention.

Blood—Hg. 85; R.B.C. 4,530,000; W.B.C. 9,300.

Differential—lymphocytes 28%. Poly. 70%; Wasserman O.

Chemistry—V.N.—21 mg. per 100 c.c. blood.

Creatinin—4 mg. per 100 c.c. blood.

X-Ray—Gall tract—No calculi opacities. ties

Stomach, duodenum, kidneys, negative.

Colon—Atonic type of stasis.

Biliary tract drainage:

Diagnostic: 125 c.c. dark, turbid bile; much mucus in gobs; pus 2 plus; Colon B. 3 plus; staphs. 2 plus; cholesterin 3 plus; few r.b.c.

Treatment — Metapyloric drainage at weekly intervals, repeated $MgSO_4$, stimuli at each seance; from 240 to 600 c.c. dark brown pus-laden bile mixtures exhibiting much bile pigment, cholesterin and rich bacterial flora recovered at various drainages. *General care*—Low fat, low protein diet; calomel; salicylates and ox bile.

Result—Liver to normal size after 3 drainages; disappearance of pancreatic tumor and local epigastric tenderness; free bile flow with pronounced reduction of abnormal elements after 4th drainage. Dyspepsia and headaches greatly alleviated. *After second gall tract drainage, psoriasis less pronounced; no lesions after 7th drainage.* Patient refused further treatment after the 9th drainage; said she was well and needed nothing further.

In summary, one has pronounced evidences of infected biliary tract, chronically enlarged liver and spleen, deficient colon function, and annoying psoriasis. The treatment suggested was non-surgical biliary tract drainage at from five to seven day intervals, a bland diet, low in protein and fat, fairly large doses of ox bile and small doses of salicylates. As the summary shows, this patient made a most excellent recovery from her dyspeptic disturbance. She abandoned treatment because she stated she was perfectly well and required no treatment.

The point which I wish to emphasize is that as this patient's biliary type of dyspepsia cleared up and as her liver and spleen returned to normal size, there was a gradual but complete disappearance of the skin lesion. Less than 4 months following the initiation of a type of therapy directed only toward restoring hepatic function, this patient had no indications whatever of what was formerly considered an incurable psoriasis. *After 9 years there has been no recurrence of the lesion.* That such obstinate skin lesion—a lesion which resisted treatment of many of our most skilful dermatologists for years—should occur in association with obvious insufficiency and gross enlargement of the liver, and should disappear permanently when the liver returned to normal size and

digestive disturbances ceased, was a clinical fact which impressed me greatly. In view of scattered observations in the literature, the inference that in some patients, at least, chronic dermatoses and deficient liver function have a relationship, seemed warranted. It was on account of this experience that, during the past 9 years, we have examined closely our biliary tract type of dyspeptics for evidence of dermatoses and have, upon the relatively few dermatological patients who have come into our practice, searched carefully for evidences of malfunction of the liver and biliary tract. A small, but suggestive group of these patients furnished the material for this report.

I realize fully that the types of skin affection observed in these patients are well known to fluctuate with respect to improvement, recrudescence and severity of lesion and that local or "constitutional" therapy as exhibited by skilled dermatologists frequently is followed by marked benefit or even cure. However, all the patients whom I am reporting had experienced long courses of management by able men, with little or no benefit. Furthermore, our material, even though it is small, indicates when judged objectively by the impartial verdict of laboratory tests that, as liver function approaches or becomes normal, skin anomalies are favorably influenced. The reverse holds true. Finally, this series suggests a different and more logical conception of what, in the dermatoses, should be regarded as faults of "constitutional," "dyspeptic," "intestinal," "putrefactive," "toxic," or "allergic" nature. It would appear that there is available a basic mechanism through which so-called "toxic" agents bring about those obstinate skin defects whose manifestations are so protean and whose management is so discouraging.

CASE REPORTS

Case No. 2. No. 6015. Mr. F. R. Age 27; attorney; born and raised in Chicago. No previous infectious disease but scarlatina as child. *Presenting complaint*—"Skin trouble"; 15 years duration, first on hands and fingers; originally at intervals, now constant. Lesion at present on face, neck, arms, body and thighs; diagnosed 11 years ago as "psoriasis and eczema". Almost constant treatment since initial lesions but no relief except slight lessening of spread. For months, lesion has been oozing, scaling, cracked and bleeding; itches worse at night. Mild, gassy "biliousness" on and off for 13 years, aggravated by over-eating but not by any special foods; is constipated; otherwise well and in good general condition.

Examination—Extensive psoriasis and eczema, mild secondary type of anemia; infected tonsils; liver three fingers below rib edge, tenderness over bile ducts; gastric secretions practically normal; stool, no parasites; sensitization tests all negative. *Biliary tract drainage*—very tardy flow, gall bladder fraction scant; microscopically, many short chained streptococci, much blood from the duodenal trauma, excessive deposit of bile salts and rich sediment of leucin. *X-ray*—marked spastic colitis; *Graham test*—poor visualization of gall bladder, with delayed emptying response.

Treatment—Frequent biliary tract drainages per duodenum; low fat, low protein diet; full doses of ox bile; small doses of salicylates; tonsils removed.

Result—Patient practically well within six months, except, during a slight "bilious" attack a year and a half ago. Has had no recurrence of skin lesion.

Case No. 3. Miss G. B. No. 5460. Referred by Dr. J. Lieberthal. Age 11, school girl; family and personal history negative; tonsillectomy at four years; right cervical abscess opened and drained at five years.

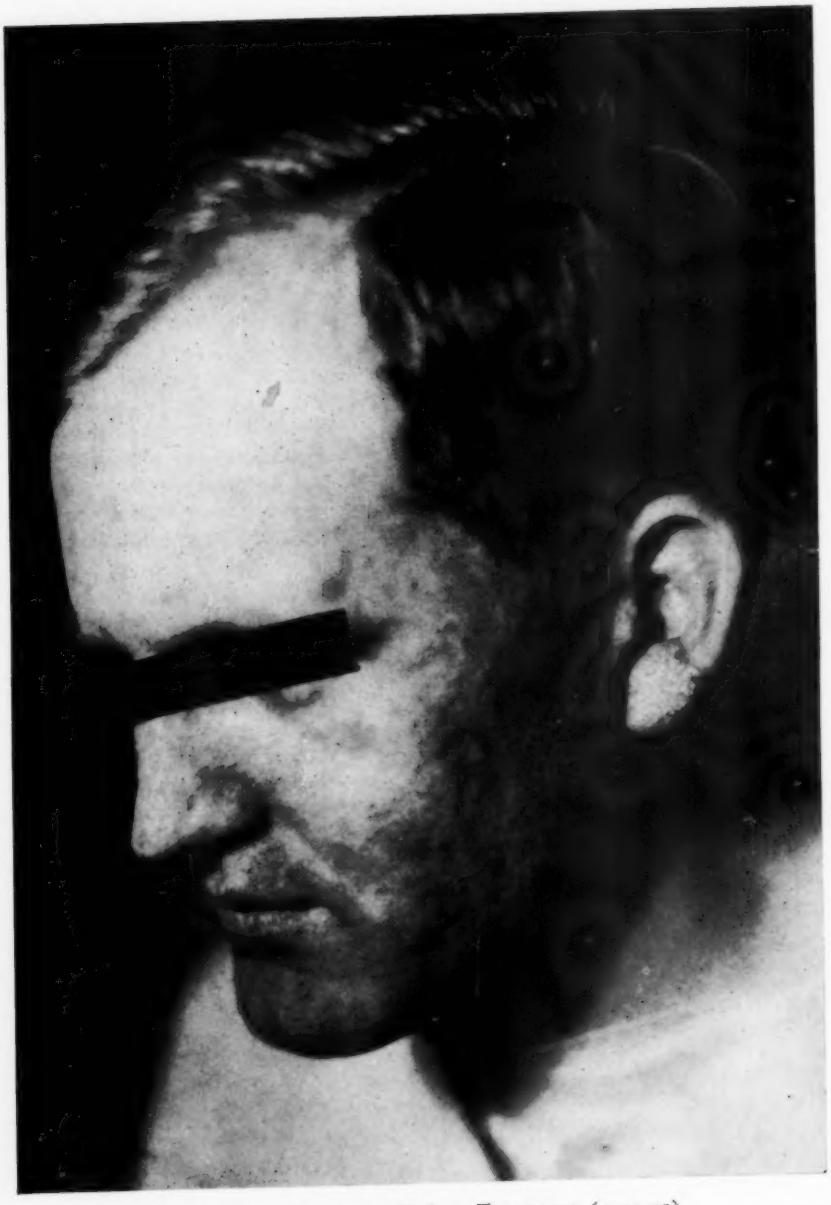

FIG. 1. Case No. 6015. Before Treatment (4-14-25).

FIG. 2. Case No. 6015. Before treatment (4-14-25).

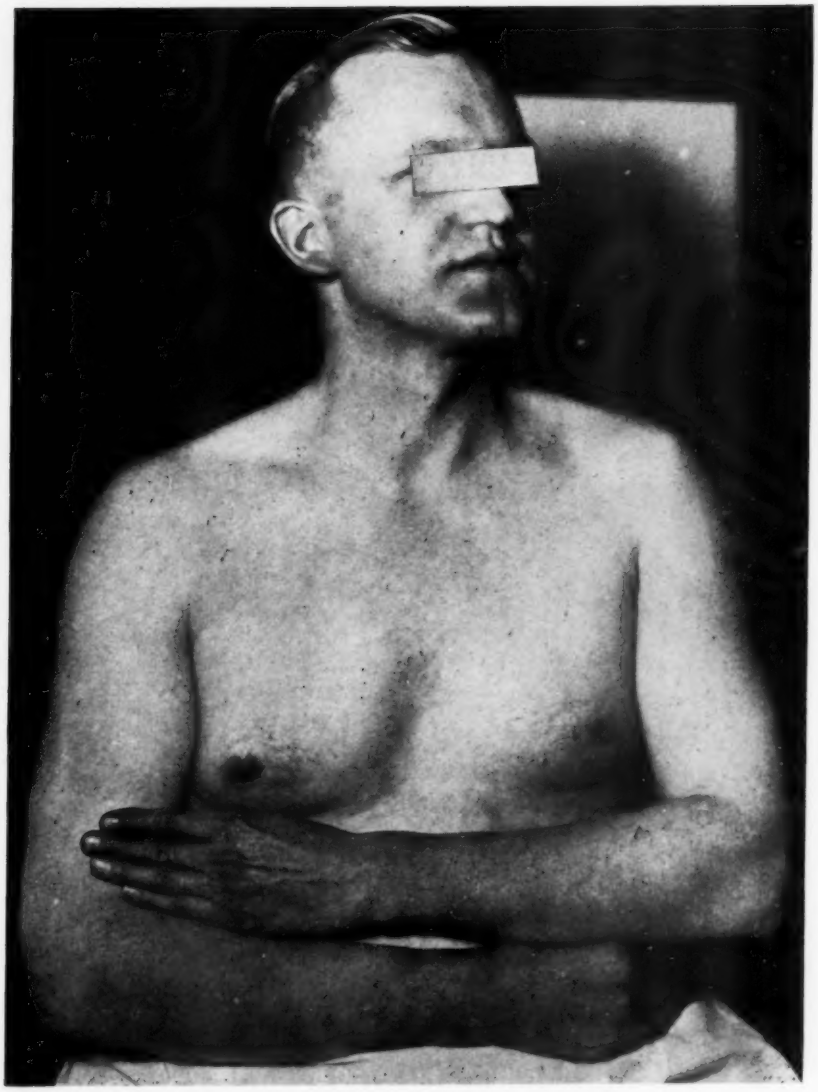

FIG. 3. Case No. 6015. After treatment (2-16-29), when patient was last observed. This photograph is practically identical with one taken six months after beginning treatment (4-14-25) and is introduced to demonstrate premanency of result.

FIG. 4. Case 6015. Before treatment (4-14-25).

FIG. 5. Case No. 6015. After treatment (7-30-25). Photographs made at later dates, up to 2-16-29 show no recrudescence of ailment.

Present complaint—"Skin trouble". Skin lesion appeared six years ago; slight eruption on face and in axilla; marked itching; would disappear for four or five days and then return; lesions at first bright red and discreet, later constant and confluent with marked inflammatory reaction; scaly, cracked and oozing skin. Has been under constant care of dermatologists and her father, who is a physician, for more than five and one-half years; unable to attend school or go about with young children on account of disfigurement.

Examination—Fairly well nourished but pale, attractive child, greatly disfigured by diffuse, exfoliative, eczematous dermatitis involving particularly face, neck, trunk and hands: skin thickened over face and neck, "pock" marked, leathery, scaly, with here and there patches of purple-red, raw confluent lesions; mucosae pale; old infected tonsils; palpable cervical and axillary lymphnodes. Thorax negative. Abdomen, definite enlargement of liver and very pronounced tenderness over the common duct and gall tract; moderate colon atony; secondary type of anemia with eosinophilia 8%. *Gall tract drainage*—Marked stasis of the entire biliary tract; pus and streptococci in siphonage; numerous "liver tubal casts" and marked excess of bile salts. *X-ray*—Colon shows marked atonic stasis.

Treatment—Acute gall tract condition warranted cholecystectomy which was performed by Dr. E. E. Henderson. Following this, liver returned to normal size and, within a month, the skin lesion about the face and neck had practically disappeared. Later Dr. Geo. Boot did tonsillectomy. Patient was placed on low-fat, low-protein diet and anti-streptococcus vaccine and salicylates administered.

Result—Progress was very satisfactory but it was not possible to keep patient under observation.

6/14/29—Has had very little treatment for the hepatic condition; all measures have been directed toward local applications to the skin. Is now young lady in high school. Moderate exfoliative dermatitis over cheeks, nose (no exudate or scaling), with scattered patches over upper thorax and lower abdomen; chest negative. Abdomen—liver comes four fingers below the right rib and spleen is palpable two fingers below the left rib margin. Blood shows moderate secondary anemia, no eosinophilia. Gall tract drainage not permitted. *Widal crisis positive response*; icterus index 20; Rosenthal not made. This patient improved noticeably when treatment was directed toward limiting gall tract stagnation and infection. When treatment was abandoned along these lines and directed wholly toward the dermatologic fault, recurrences followed. Obvious chronic embarrassment to liver function are shown by constantly enlarging liver and spleen, a positive Widal crisis and high icterus index.

Case No. 4. Mrs. M. No. 2310, age 55. Family history negative. Personal history—quinsy, mid-life; rheumatic fever early life; appendectomy at four years of age; pelvic operation 38 years of age.

Presenting Complaint—Chronic diffuse skin lesion diagnosed and treated for many years as psoriasis; muscular weakness; "liver trouble"; constipation. For more than 25 years has had irregular attacks of "biliousness". Eighteen years ago, had a cholecystostomy and was told that liver was enlarged. Skin lesions appeared several years following her first attack of "biliousness" and have been present on and off ever since. States that with, or following, "bilious" attacks, skin lesion always more extensive and more annoying and seems to "spread". Says new lesions always appear in association with digestive upset. Obstinate constipation last four years aggravated by weak perineum.

Examination—Stocky, fairly well nourished, somewhat anemic, middle-aged woman with unsightly, extensive, scaly, pinkish red patches of psoriasis at elbows, thighs, knees and neck. Moderate cardiac enlargement without hypertension. Abdomen — liver descends three fingers below right rib in anterior axillary line, tender to pressure, tenderness passing up along the common bile duct; distended right half of colon; hemorrhoids; marked rectocele. *Graham test* shows poorly visualized gall bladder with calculi opacities; barium enema—marked colon atony. Test meal—free acid 19, total

FIG. 6. Case No. 5460. Before treatment (6-7-24).

37. *Gall tract drainage*—marked hepatic duct stasis; aspirates contain pus, excess of cocci and colon bacilli and bile salts. Blood nitrogen 18, blood sugar 120. Sensitization tests—all antigens negative.

Treatment—The gall bladder was removed surgically and long continued drainage through tube in common duct instituted. Later, at irregular intervals, duodenal drainage performed with evident relief of dyspeptic symptoms and definite with regard to skin lesions. However, normal liver fractions never secured at siphonage. Rosenthal 30, icterus index 16, three years after cholecystectomy. At that time, blood nitrogen 12, blood sugar 90. Colon still showed general atony.

Result—Skin lesions practically disappeared permanently over neck and arms but persisted moderately with fairly severe exacerbations, however, over thighs and legs.

Case No. 5. Mr. A. D. Age 43, No. 8389. Merchant.

Presenting Complaint—"Gassy" type of dyspepsia for more than three years; severe "hives" and "boils" for the past two and one-half years. Family and personal history practically negative; no occupational hazard. Has had irregular, recurrent attacks of "biliousness" for more than three years; eructations of gas, slight vomiting and definite distress in the right upper quadrant. About six months after first 'bilious" attack, noticed itching of skin and large "hives" appeared, usually some time after eating and particularly at night. Itching was intolerable. Some of the "hives" became infected (?) and "boils" followed. Sought relief from dermatologists and internists and has been under close medical observation for more than two years. The condition seems

FIG. 7. Case No. 5460. After cholecystostomy (7-7-25).

to be worse at present. Is constipated; general health good.

Examination—Very pronounced erythemic rashes over the entire body; marked dermatographia; infected wheals on left shoulder, lower abdomen and in axilla. Infected tonsils. Thorax negative. Abdomen—liver not felt; definite tenderness over theoretic gall bladder and bile duct zones. Spastic descending colon. *X-ray*—Graham tests: poorly visualized gall-bladder; barium enema—very spastic colon, generally. *Stool* negative. *Gall tract drainage*—Moderate biliary tract stasis; hepatic fraction secured sluggishly but contains short chained streptococci and moderate excess of cuboidal epithelium. Rosenthal 18, icterus index 16; blood nitrogen 21, blood sugar 143. *Sensitization test*—all antigens negative.

Treatment—Fifteen non-surgical biliary tract drainages, first, at five day intervals and later, at two week intervals. Last drainage, free flow of all bile-passage fractions with practically negative microscopic examinations. Rosenthal 10, icterus index 7; blood nitrogen 12, blood sugar 84. Graham test; practically normal shadow with exception of duodenal adhesion; barium enema—no objective anomaly.

Result—Complete recovery from urticaria and "boils" after four months. There has been no recurrence after one and one-half years.

Case No. 6. Mrs. F. O. Age 43, No. 8049, Housewife.

Presenting Complaint—"Bilious" type of dyspepsia of fifteen years duration, at intervals; recurrent attacks of acne rosacea, with eczematous exacerbations; skin lesion present over fifteen plus years. *Family and personal history*, practically negative except for mild diphtheria and scarlatina as a child. Dyspeptic disturbance on and off for 15 plus years manifested by "up-pressure" sensation in epigastrium, marked eructations and occasional pyrosis; is constipated; has lost thirty pounds weight in one and one-half years. During the past ten years, has been under dermatologist's care for skin affection but there has been no permanent result. Says that skin condition is always worse preceding or during attacks of "biliousness"; in fact, frequently can tell when she is about to be "bilious" because of rather sudden exacerbations of skin lesions.

Examination—Woman in good flesh, exhibiting mild anemia; rather marked lesions of acne rosacea over face and neck; some of these lesions discrete, very deep red, not purulent, while others are confluent; considerable general edema of skin of neck and face; mucous surfaces clean; tonsils infected. Heart and lungs normal. Abdomen—liver just felt at right rib edge; definite spasm along the theoretic course of common bile duct and over the gall bladder. Distended cecum and ascending colon; spastic descending colon; ulcerated fissures in anal canal; small bleeding hemorrhoids. Stomach contents free HCI 12, total 24, no gastric retention. Stool negative. *Gall tract drainage*—very pronounced stasis in hepatic ducts and in gall bladder; fractions removed are rich with streptococci and colon bacilli, with blood, (duodenal trauma?), cuboidal epithelium and bile salts; *Graham test*—gall bladder barely visualized; no calculi shadows. *Barium enema*—spastic colon; mild chronic ulcerative colitis. Rosenthal 15; icterus index 18 to 16; Widal crisis not observed; blood nitrogen 14, blood sugar 118. Sensitization tests, all antigens negative.

Treatment—Frequent non-surgical biliary tract drainages; low fat, low-protein diet; full doses of ox bile; fourteen gall tract drainages in all. *At last session*, 475 c. c. recovered, particularly from the hepatic duct radicals; microscopically, it was practically negative. Rosenthal was 15 to 20; icterus index 6 to 12; Widal crisis suggestive positive; blood nitrogen 4.2, blood sugar 80. Graham test—poor visualization of gall bladder; barium enema—spastic descending colon.

Result—Fairly good, only one recurrence during past three years of management. This patient is socially inclined, is very hard to manage with respect to biliary tract drainage, diet and medicine. At present, while a few acne lesions remain, general skin condition is excellent and in no wise deforming.

Case No. 7. Mr. B. C., Age 62, No. 8488, Attorney.

Present Complaint—Irregular attacks of "liver" trouble for the past twenty-five years; obstinate "hives" and sudden swelling of tongue and mucous membranes of throat; the latter disturbance interferes with his profession and at times threatens suffocation. The skin and mucous membrane lesion has been present slightly for more than twenty years, but during the past eight months, has been constant. Patient has spent most of the past eight months in hospitals, having sensitization tests made and experimenting with various forms of dietetic regime. There has been no result except when he was on rice and water. At such time, had no "hives" or mucous membrane lesions, but lost weight so rapidly and became so weak that physical collapse was threatened. *Family and personal* history negative with exception of patient having typhoid fever as a youth.

Examination—Florid, undernourished, medium sized male with rather marked facial asymmetry, fulness of the right face being due to edema; tongue could be only partly protruded on account of its being swollen. Large "hives" and (urticaria) wheals over shoulders, in axilla, over abdomen and along inner surface of thighs. *Mouth*—edema is present, not only of tongue but in soft palate, patient's voice being muffled and "thick"; both tonsils of buried type and infected. *Thorax*: moderate cardiac hypertrophy, aortic enlargement; blood pressure 154/88; peripheral vessels—moderate arteriosclerosis; lungs clears. *Abdomen*—liver palpable in right anterior axillary line; very pronounced resistance over theoretic gall bladder zone and along common bile duct; dilated cecum and ascending colon. Test meal—free HCl 20, total 44, *Graham test*—large mottled gall bladder shadow; *barium enema*—marked degree of atonic colitis. *Gall tract drainage* — Pronounced stasis, particularly in hepatic ducts; siphonage shows microscopically a marked excess of bile salts. Rosenthal 50; icterus index 20 to 16; Widal crisis highly suggestive positive; blood nitrogen 17; blood sugar 67. *Sensitization test*—all antigens negative.

Treatment—Biliary tract drainage per duodenum every fifth day at first and then, later, every two weeks; twenty-five drainages in all. *At last drainage,* more than 1000 c.c., mainly hepatic duct bile, were secured. Microscopically, it was negative. Rosenthal 20, icterus index 8; blood nitrogen 6.1; blood sugar 88; *Graham test*—atonic gall bladder containing calculi; colon enema —normal haustral markings.

Result — Excellent; no recurrence of hives, urticaria or mucous membrane oedema after seven gall tract drainages; patient has been symptom-free so far as skin and mucous membrance disturbance for more than one and one-fourth years. Is still on low-protein diet and has occasional "rounds" of calomel and ox bile.

Case No. 8. Mrs. R. B. Age 40; No. 8974. Housewife.

Presenting Complaint—"Skin trouble," constant, one year; mild irregular gassy type of dyspepsia about two years. *Family and personal history,* negative except mother died of diabetes. During the past two years at irregular intervals has been mildly "bilious"; full feeling in epigastrium, eructations, feeling of weakness and some nausea; has been constipated. About a year since, quite suddenly, developed red blotches over skin; these spread rapidly and became confluent, itched, broke and discharged and, at times bled. When healing took place, scaliness followed; skin has never been normal since first appearance of lesion and the itching, particularly at night, has interfered with sleep and made patient very nervous. Has consulted leading dermatologists. The lesion has been pronounced "psoriasis and eczema."

Examination—An overweight middle-aged woman of myxedematous cast with extensive scaly covered eruptions on legs and knees, with irregular confluent patches of flat erythematous lesions on thighs; confluent pinkish lesions over hands and arms, some covered with fine scales and others fissured and bleeding; very pronounced changes of similar character over face and particularly the neck and upper thorax. About the mouth and on the neck the lesions are granular and fissured and exude an abundant sero-sanguinous fluid. Eyes and mouth negative, except for infected right tonsil. Thorax—myocardial weakness, mod-

erate dilatation; lungs clear; blood pressure systolic 98, diastolic 66. *Abdomen*; liver just palpated at rib edge in right anterior axillary line; possible tenderness over the course of the common bile duct and gall bladder; very pronounced dilatation of colon, particularly right half. Painful intersphincteric anal fissures; pelvic examination negative. Test meal (difficult to obtain) free HCl "present". Blood examination—hemoglobin 70%, r.b.c. 3,900,000, w.b.c. 6,400; stool negative. *Gall tract drainage*—very sluggish flow, no liver fraction being obtained; microscopically negative; *Graham Test*—gall bladder poor visualized, no calculi shadows, liver enlarged; barium enema—general colon atony. Rosenthal 20 to 22; icterus index 12 to 20; Widal crisis highly suggestive positive; blood nitrogen 9, blood sugar 105; Sensitization tests—negative to 52 antigens except slight positive response to timothy and goose feathers.

Treatment—Biliary tract drainages first at five day intervals, later two weeks, twenty in all. *Last drainage*, only fairly free, 160 c.c. of common duct and gall bladder bile secured with practically no liver fraction; microscopically negative. *Graham test*—fairly clear gall bladder shadows; liver shadow very dense; barium enema—normal haustral markings. After treatment—Rosenthal 15, icterus index 9 to 12; Widal crisis suggestive negative response; blood nitrogen 4.2; blood sugar 70; red blood cell 4,800,000 with hemoglobin 80%.

Result—Very pronounced improvement of lesions over face, neck, thorax and fair result over legs and hands. Subject is a very difficult patient to manage and neglects dietetic and medicinal treatment. Exacerbations over hands and legs nearly always associated with mild digestive upset.

Case No. 9. Mrs. C. age 40; No. 9272. Housewife.

Presenting Complaint—Severe "eczema" of both hands; mild "biliousness". Family history negative. Personal history negative except for severe attack of grippe during war time. Skin lesion first appeared about two and one-half years ago. She was pregnant at the time and during this pregnancy was unusually ill with "bilious attacks," nausea, vomiting and prostration; placenta previa was diagnosed. *Skin lesion* first appeared on hands during latter part of pregnancy, rapidly spread to arms; fingers swelled, skin cracked, oozing occurred and, in many places, lesion open, red and raw. Consulted dermatologists with some relief but condition never cleared up; hands continued to swell so that rings could not be worn, fists made, or fingers extended beyond two-thirds normal. Dyspepsia has never been severe but has been more or less constant. She is mildly constipated.

Examination—Over all fingers and the palms of hands and between fingers, diffuse ulcerative, weeping, scaly eczematoid lesions; marked general skin edema, rather typical general cellulitis; patient has to wear gloves constantly on account of deformity and for protection. Teeth well repaired, negative; small buried, infected tonsils. Lungs and heart negative; blood pressure 128, diastolic 76. *Abdomen*—liver descends two fingers below the rib edge at right anterior axillary line; very marked tenderness in gall bladder zone; cecum greatly dilated; rectal—external, fissured hemorrhoids; pelvis negative. *Test meal*—free HCl "present"; stool negative except for occult blood, positive. Blood—hemoglobin 80%, r.b.c. 4,200,000, w.b.c. 7,600; eosinophiles 2%. *Graham test*—only a slight visualization of gall bladder; liver large and dense. Colon enema—general atony and dilatation; "cess pool" cecum. *Gall tract drainage*—Marked stasis, scarcely any gall bladder fraction being secured; microscopically the siphonate exhibits leucocytes in excess, numerous streptococci and moderate excess of bile salts. Rosenthal 30, icterus index 20 to 15; Widal crisis highly suggestive positive; blood nitrogen 16; blood sugar 115. Sensitization tests—all antigens negative.

Treatment—Gall tract drainage at 5 to 8 day intervals. *Last drainage*: rapid drainage of 375 c.c. containing all bile tract fractions and negative mircoscopically. *Graham test* shows well formed gall bladder shadow. Barium enema—no stasis, haustra are appearing. Rosenthal 15, icterus index 8, Widal crisis suggestive negative response; blood nitrogen 14, blood sugar 82.

FIG. 8. Case No. 8974. Before treatment (7-6-27).

FIG. 9. Case No. 8974. After treatment (2-12-29). Photograph shows permanent result.

Fig. 10. Case No. 8974. Before treatment (7-6-27).

FIG. 11. Case No. 874. After treatment (2-12-29). Photograph introduced to demonstrate permanency of result.

FIG. 12. Case No. 972. Before treatment (2-4-29). Lesion had been constant and progressive for nearly two years. Note cellulitis and open, discharging ulcers. Patient unable to extend fingers more than shown in photograph.

Fig. 13. Case No. 9272. After treatment (6-22-29). Note full extension of fingers, disappearance of edema and swelling, natural texture of skin and almost complete healing of previously intractable ulcers. (Recovery complete when seen 7-18-29.)

FIG. 14. Case No. 9272. Before treatment (2-24-39). Ends of fingers could not be included in photograph because cellulitis did not admit of greater extension.

FIG. 15. Case No. 9272. After treatment (6-22-29). Note normal extension of fingers, healed ulcers and disappearance of cellulitis. Patient able to wear wedding ring for first time in two years. Result permanent (11-27-29).

FIG. 16. Case No. 8389. Before treatment. Marked "hives" and dermatographia (12-6-26). No lesions present 8-12-29.

Result—Most striking improvement after second gall tract drainage; hands practically well, skin returning to normal texture; can wear wedding ring for first time in two years and can open and close hands normally.

Summary: Of the nine patients—three were males and six were females, one of the latter, a child. With this exception, all were in adult life. These adults had been dyspeptics for an average period of approximately 14 years, a range of from 2 to 25 years. The child had always been a feeding problem.

The Characteristics of the Dyspeptic Disturbance were strikingly similar: irregular or constant "gassy" indigestion, bloating, nausea, epigastric distress soon after meals (particularly heavy or complicated meals), rarely, acute discomfort. In other words, "biliousness," or translated into clinico-pathologic phraseology, chronically infected, poorly-draining gall bladder and bile ducts with associated hepatitis. Before coming under my observation, two of the patients already had experienced standard operations upon the biliary passages by surgeons of repute. Except as such operations averted acute and dangerous crises, no permanent benefit had followed. Case 3 (No. 5640—the child) was operated upon at my suggestion; the effect of this operation upon the dermatosis was striking and will be commented upon later.

All the patients of this series were costive, several distressingly so. As with many instances of intestinal stasis, constipation doubtless, in large measure, was due to deficient or faulty type of food intake in the effort to avoid dyspeptic storms. This food imbalance is a factor not to be disregarded in its effect upon preparing the "skin soil" for the subsequent development of dermatoses. All are familiar with the dermatologic aspects common to such "deficiency" diseases as pellagra, sprue, scurvy, etc.

The skin lesions exhibited were all of chronic type. My own limitations in dermatologic nomenclature are admitted, but, for so many years had these patients been under the management of skilled specialists, that the descriptive names of skin lesions given by their dermatologists had been thoroughly agreed upon as "eczema," "psoriasis," "acne rosacea," "urticaria"—lesions which, as Arthur Whitfield[1] says, are "a type of reaction rather than disease" and W. A. Pusey[2] considers a "group of toxic disturbances, producing in one instance urticaria and another eczema." Seven of my patients had, with Job-like patience, endured the physical suffering and the mental anguish of eczematous dermatoses for an average of approximately 9 years (a range of from 1 to 23 years). The two instances of urticaria ("hives" "boils") had been afflicted respectively 2½ and 20 years; in the latter instance, to an incapacitating degree for longer than 8 months.

In all patients, the lesions were so extensive and deforming as to prevent the subjects' going about socially or actively conducting business affairs. In two patients, the mental reaction was sufficiently morbid to bring frequent expressions of suicidal intent. One of the urticarial subjects was being driven from an important consulting law practice and, on account of sudden swellings of tongue and

soft palate, lived in dread of suffocation. The psychic and the economic status of these sufferers had not been improved by going from one specialist to another and trying scores of salves, lotions, lamps and diets.

Relationship of "liver type" of dyspepsia to skin lesions: It is important to record that in none of our patients was there a family history of skin affection. While it is claimed by numerous dermatologists, Bloch,[3] Klauder,[4] Murray,[5] Ormsby,[6] that individuals who develop chronic dermatoses have a constitutional predisposition to such—i.e. "the soil" is suitable and is different from that of the majority of humans, yet in this series, none of the patients had a skin lesion prior to the inception of a type of dyspepsia, which, to laity and profession alike, is associated with defective liver and bile duct function. As I have mentioned, the average duration of the skin lesion was 9 years. The correlation of the two affections, frequently was striking: case 3091—a long-term bilious dyspeptic, but with absent skin lesions until noticeable enlargement of the liver appeared; case 5460—a rather acute biliary tract flare-up, with almost complete relief of eczema when liver function became normal—but, as hepatitis developed (with, in 1929, splenic enlargement)—constant and extensive recrudescence of dermatosis; case 9270—a mildly "bilious" dyspeptic, who, during pregnancy, had violent gastric upsets, and who, at this time, developed an eczema of great severity—are instances similar to those conditions mentioned by Couinary and Cloque[7] and Crainicianu and Popper.[8] Furthermore, almost without exception, and certainly while they were under my observation, patients noted that exacerbations of their dermatoses occurred in close proximity to "bilious" attacks; in fact, case 2310, would come in for treatment of her dyspepsia actually before she was ill, and in order to anticipate distress, because the flaring up of her psoriasis warned her by experience that soon she would have a "bilious" attack.

OBJECTIVE EVIDENCE OF DISTURBED LIVER AND BILIARY TRACT FUNCTION:

(1) *Liver Enlargement and Gall Tract Tenderness*:

With one exception, (Case 8389—an instance of urticaria) all the patients had easily palpable livers. In three patients, the livers extended from 2 to 5 fingers' breadths below the right rib margins, and were tender to touch. The livers were smooth-surfaced and gave the palpating fingers the impression of being inflammatorily engorged. (Table 1) So-called "biliary tract" tenderness was very definite and local in all patients, even in the patient who did not exhibit palpable liver. Four patients complained of such degree of distress upon palpation as to give the impression of an acute or advanced sub-acute lesion being present. Carnett's[9] tests indicative of definite visceral, in contradistinction to parietal tenderness, were all positive. In case 5460—the child—the degree of localized upper quadrant tenderness, taken into consideration with dyspeptic history and enlarged liver, determined operative interference.

(2) *Roentgen Proof of Biliary Tract Anomalies*: Upon 7 patients it

was possible to carry out the Graham roentgenologic routine. (Case 3091 had had cholecystectomy before coming under observation and case 5460 was deemed to be an unsuited subject). In all 7 subjects, the returns were "Graham positive," the resulting films demonstrating sluggishly filling and emptying gall bladders, with or without calculi. Roentgenologically, three patients exhibited large livers (Cases 3091, 8974, 9282). Where carried out, the roentgen study, in all instances, corroborated the facts suggested by clinical history and physical examination. (Table 1).

(3) *Metapyloric Intubation and Biliary Tract Drainage*: To those with experience, there is no longer doubt regarding the usefulness of Lyon's procedure for investigating the ability of the gall-bladder and ducts to discharge their contents and, from the material obtained, to secure information of value relative to disturbed liver and biliary tract function. The recent contributions of Lyon[10] (in collaboration with Manges), and Bockus[11] demonstrate the clinical importance of duodenal intubation. Piersol, Bockus and Shay[12] have shown that the procedure is of greater diagnostic worth in gall-stone disease than are clinical examinations and the Graham test. In treatment of urticaria, Menagh[13] has attested its importance. More than 15,000 duodenal intubations performed by my associates and me support the observations of these investigations.

In the series of dermatoses comprising this report, duodenal intubation was performed upon each patient as a diagnostic procedure and upon all patients but one (No. 5460—the child) as a therapeutic measure. Table 1 summarizes our experiences at diagnostic intubation.

In all instances, the siphonates, (after spaced instillations of 33% warm $MgSO_4$ solution into the duodenum), were scant and tardy or non-classical flow was observed. From cases Nos. 2310 and 8974 (both instances of extensive eczema) we secured no hepatic duct fractions; each had a palpable liver.

Cases Nos. 8049, 8488 and 9272 exhibited stasis of both gall-bladder and hepatic bile-ducts. These observations, made before Graham tests were carried out, were in entire agreement with that roentgenologic manoeuvre. At none of the diagnostic intubations, was a total of greater than 100 c.c. of bile admixtures secured, and at no session upon any patient was the classic sequence of biliary tract fractions recorded.

The microscopic examination of the siphonates demonstrated abundant evidences of vesicle and duct pathology; leucocytes in excess, short chain streptococci foreign to the normal biliary trace (5 patients) exfoliated cuboidal epithelium (actual liver duct "casts," in case 5460), and, with one exception (case 8389—an instance of severe urticaria), rich sediment of bile salts (from case 6015—extensive psoriasis and "eczema"—an abundance of leucin plates). Associated with the biliary tract dysfunction, three patients (Nos. 3091, 6015, 8049) exhibited definite duodenitis, with spastic viscera, engorged and easily bleeding.

It is thus apparent that, in this group of dermatoses, duodenal intuba-

tion not only supported clinical and roentgenologic evidences of gall-bladder and duct disease but amplified those observations by demonstrating faulty hepatic function.

(4) *Special Observations upon the Functional Integrity of the Liver*: To secure further proof of the presence or absence of liver damage, we made, where possible, a study of the excretory capacity of the liver by Rosenthal's dye test and estimated the icterus index. In an attempt to gauge its "buffer" (Opie,[14] "barrier" or protopexic Widal,[15] et al functions, we carried out "Widal crisis" studies upon four patients—in two before and after treatment—and, in the fourth, only in connection with a "check up" several years after the patient (Case No. 5460) first had been seen. As additional evidences, upon most patients we estimated blood nitrogen and blood sugar values before and after management. Unfortunately, we have no observations to report relative indicanemia and variations in urobilinuria (Rowntree, Green and Aldrich,[16] Cabrini[57] Bauer and Nyiri.[18]) Neither was there opportunity to record fluctuations in the hydrogen-ion concentration of the blood as suggested in the dermatoses by Levin and Kahn,[19] Sweitzer and Michelson,[20] Drouet and Verain,[21] and by Bertacini.[22]

Liver Function Tests: One should have a clear idea as to the significance of the various tests in vogue to evaluate hepatic function. The literature is rich with reports upon the "comparative" worth of numerous procedures. Often enough, comparisons or contrasts are made between tests which are in no wise indicative of similar physiological functions of the liver. (vide—Rubenstone and Tuft,[23] Gonzalez and Karr.[24]) In a measure, the liver can be tested with regard to its capacity for bile formation and excretion (Rosenthal, icterus index) and with respect its "buffer" or "barrier" function (Widal's "crisis"—an imperfect procedure, perhaps, and yet one which broadens our conception of the viscus as a physiologic "dam" against noxious agents carried to it from the alimentary tract.) These functions cannot be compared by one set of tests.

Evidence supplied by Suzuki and Sato[25] appears to indicate that the liver also possesses a specific detoxicating hormone, particularly manifested against foreign protein and thus preventing anaphylactic shock. In certain individuals, this hormone is not available or is of reduced value when the parenchyma of the liver is injured. Liver damage—intrinsic and extrinsic—disturbs all its complicated activities: the metabolism of carbohydrate and protein and the formation of bilirubin. Such disturbance follows almost constantly, to great or less degree, upon disease of the biliary passages (Rous and Larimore,[26] Brulet and Garban,[27]) and lesions of the alimentary tract (Ehrmann,[28] Warner,[29] Galloway,[30] Larat and Siebenman,[31] Menagh[13]).

In this series, Rosenthal tests were performed upon five patients before and after management, and in one case where treatment had been carried out but indifferently. Before therapy, the average Rosenthal was 25 with a range of 15 to 50. These are not especially indicative of marked delay in the ex-

cretory capacity of the liver, for the dye used. The highest figure (Case No. 8488) was returned by a patient affected with most incapacitating urticaria and where Graham Test and duodenal intubation indicated gall stones and most marked hepatic duct stasis. Another high figure (Case No. 9272) was recorded where seemingly definite liver embarrassment, with subsequent eczema, was associated with pregnancy.

The Icterus Index for the series averaged approximately 17, a definite increase over figures returned from normal livers. Several patients, whose livers, clinically, were abnormal exhibited fluctuations in their indices (Cases Nos. 8974, 9272, 8488)—suggesting that liver reserve was available and could be exhibited automatically. Upon those patients who were insufficiently treated icterus indices remained higher than the normal average.

"Widal Crisis": Four patients were available for "crisis" observation before treatment and two of these had comparative studies following fairly well supervised management. We did not regard absence of digestive leucocytosis alone as a criterion for a positive "shock" but considered leucocyte variations in association with increase in coagulation time and fall in blood pressure over a period of 100 minutes in our interpretation.

Widal and his co-workers maintain that the normal liver arrests the incompletely digested proteins which come from the intestines by way of the portal blood; it completes the protein metabolism and then passes on into the vena cava the harmless end digestion products. If the liver is diseased, however, the imperfectly split proteins pass through the liver into the general circulation, where parenteral digestion is carried forward by blood enzymes. In 1912, I[32] showed that normal blood serum could split glycyltryptophan. The presence of these "foreign proteins" in the general circulation is followed by "shock" as they are split, this "shock" manifesting itself by leucocyte and blood pressure drop and by increase in the blood coagulation time. If, to a patient with a liver diseased in such fashion that the "barrier" function to protein is deficient, a simple albumin solution (as 200 grams of milk) or a concentrated protein (as cheese) be fed, the rapid passage of the incompletely split protein, through the liver to the general circulation, is often followed by absence of digestion leococytosis and by the objective and subjective phenomena roughly comparable to what occurs where egg white or peptone is given intravenously. It is quite likely, as suggested by Mauriac,[33] that the manifestations of Widal's "Crisis" are modified by variations in the integrity of the stomach and the intestines, particularly the jejunium.

"Allergy" and "anaphylaxis" are terms commonly employed to explain the origin of many dermatoses of intrinsic origin. Dermatologic literature is replete with articles emphasizing that, in certain subjects, unsuited diet, particularly when such is associated with "digestive disorders" is responsible for sensitization and the resultant skin lesions. However, only occasionally does one find a hint as to *by what mechanism*, the improper food or its

split products in the alimentary tract produces the allergic state. Therapy for the dermatoses almost invariably includes a dietetic regimen, usually suggested without foundation other than the dermatologist's accumulated experience, or broadly advised along the lines of less *total food* intake, greater fluid, and free opening of the bowels: good practical rules, often very effective, particularly when the patient further is advised to abandon all those foods which he has found to aggravate his eczema or his urticaria (vide Case No. 8488, who was almost symptom-free upon rice gruel, but who nearly collapsed from malnutrition upon this diet.) A few dermatologists have appreciated the rôle of the defective liver in the production of the "allergic" state, notably Bruno Bloch,[3] von Deschwanden,[34] Lehner, Rajka and Torok,[35] Menagh[13] and Goffredo del Vivo.[36] They emphasize the facts that in individuals of a certain constitutional type, the passage through the liver of protein substances (and possibly chemical groups of non-protein nature) which have not been detoxicated, is responsible for localized skin "sensitization" with resultant dermatologic manifestations. These may be of widely different character and degree: clinically, they furnish the great group of intrinsic or "endogenous" dermatoses called by various descriptive terms, urticaria, eczema, psoriasis and the like. The histologic and physical changes in the liver and the skin, particularly in the capillary bed, have been painstakingly investigated by Manwaring (peptone "shock")[37] and by Grant[38] (urticarial reaction). This and our conception of the relationship of the liver and of the alimentary tract permits a broader and possibly more hopeful view of the chronic dermatoses than is afforded when skin lesions are considered only from the standpoint of local deformities to be treated and when "internal" management is along rule of thumb lines.

In three of our patients, (Cases Nos. 8488, 8974, 9272) Widal "Crises" were platted as highly suggestive positives (Charts I, II, III). This record was in harmony with other evidence already detailed, indicating deficient liver function.

Blood nitrogen was estimated per 100 c.c. of blood in 7 of our patients: it averaged approximately 16.5, with a range of from 9 to 21.2. These rather high returns would appear further to substantiate the opinion that the liver "barrier" function was deficient. Strumpke and Soika[39] and Pezzali[40] recently have commented upon the increase in residual nitrogen in the dermatoses, and where liver function is impaired, Fiessinger, Oliver and Herbain[41] have formulated an index of blood deamination as a test of hepatic integrity.

Blood Sugar Estimations were recorded before treatment in 8 of our patients. The average per 100 c.c. of blood was approximately 113, mmgm. a range for the individual of 67 to 143. The high blood sugar values, not associated with glycosuria, certainly are suggestive for deficient sugar metabolism and glycogen storage by the liver. Such findings, in association with chronic skin lesions, have been commented upon frequently, most recently

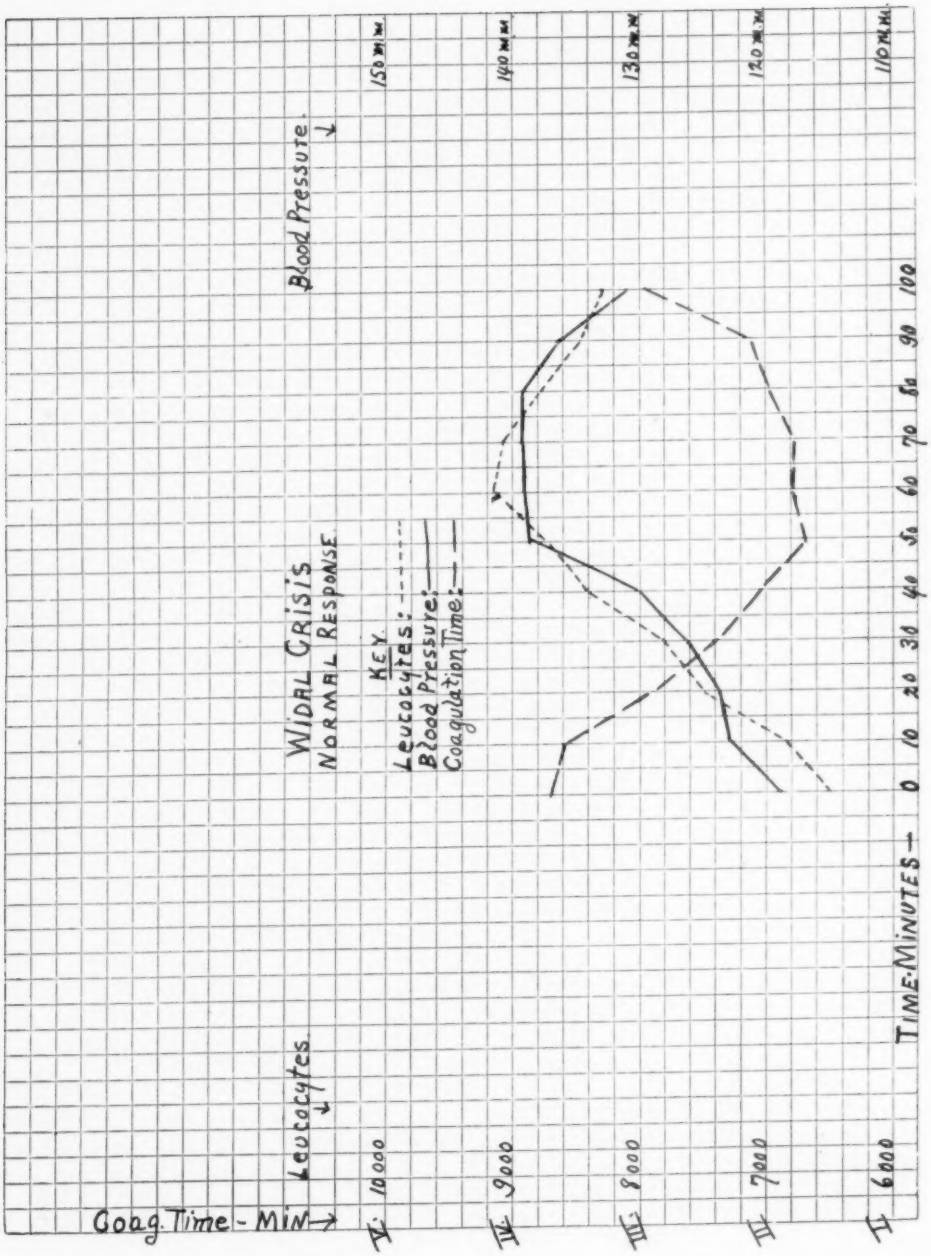
Blood Pressure
WIDAL CRISIS
NORMAL RESPONSE
KEY
Leucocytes:
Blood Pressure:
Coagulation Time:
Leucocytes
Coag. Time - Min
150 m.m.
140 m.m.
130 m.m.
120 m.m.
110 m.m.
10,000
9000
8000
7000
6000
TIME-MINUTES — 0 10 20 30 40 50 60 70 80 90 100

CHART I

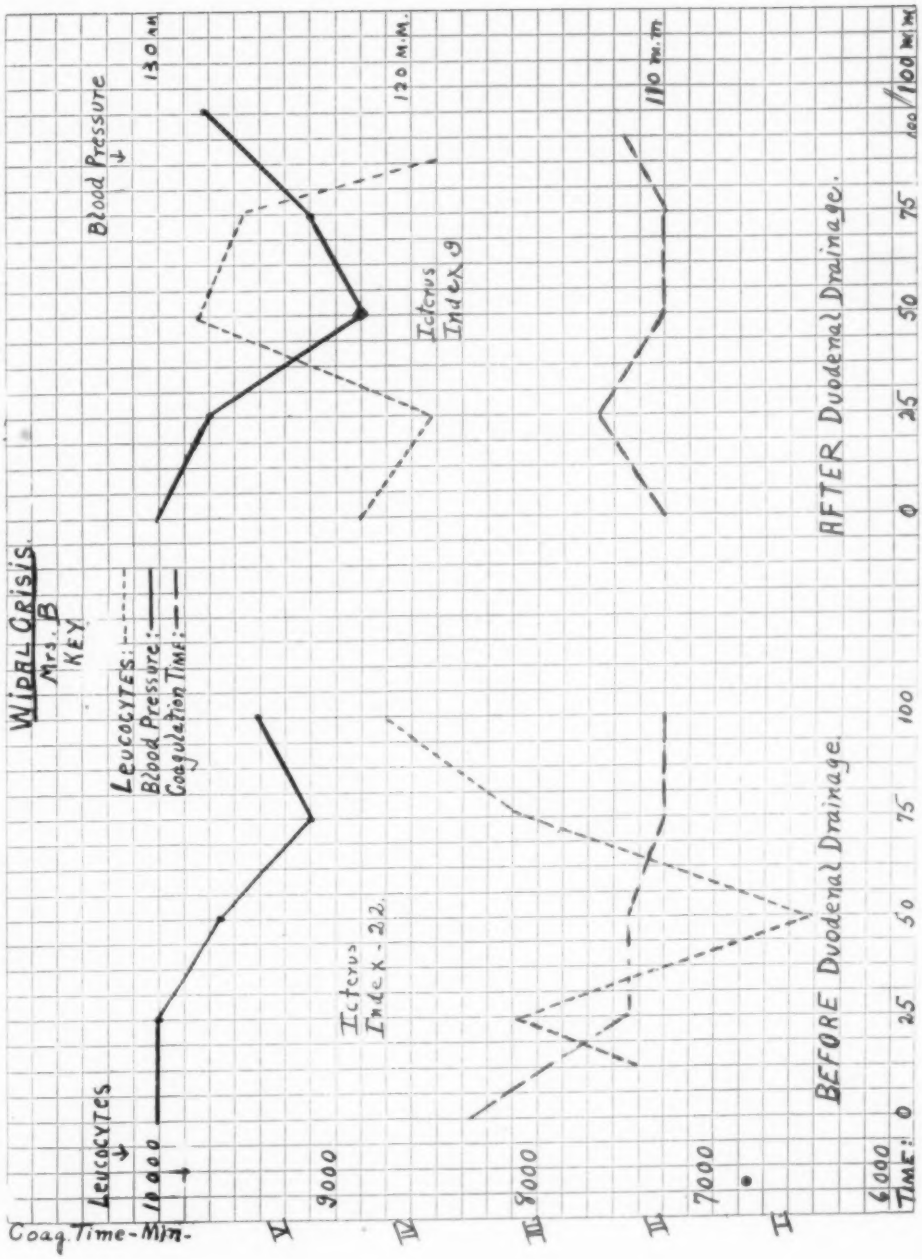
WIDAL CRISIS
Mrs. B
KEY
LEUCOCYTES: ------
Blood Pressure: ——
Coagulation Time: — —
Blood Pressure
130 M.M.
120 M.M.
110 M.M.
Icterus Index 9
Icterus Index - 22.
LEUCOCYTES
10000
9000
9000
7000
6000
Coag Time-Min-
V
IV
III
II
I
TIME: 0 25 50 75 100
BEFORE Duodenal Drainage.
0 25 50 75 100
AFTER Duodenal Drainage.

CHART II

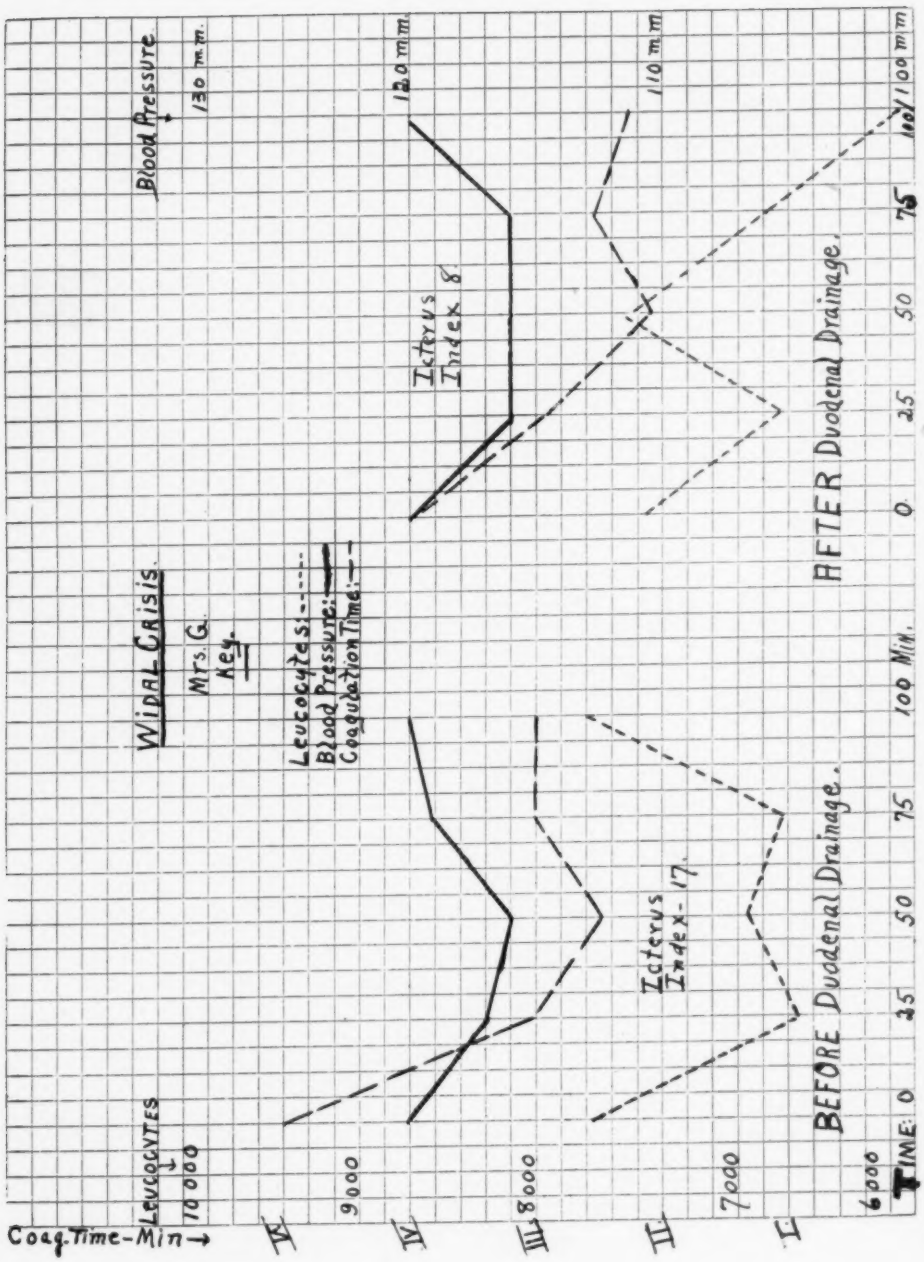
Widal Crisis.
Mrs. G.
Key.
Leucocytes:
Blood Pressure:
Coagulation Time:
Blood Pressure
130 m.m.
Coag. Time - Min ↓
Leucocytes ↓
10 000
9000
8000
7000
6000
TIME: 0
25
50
75
100 Min.
0
25
50
75
100 m.m.
110 m.m.
120 m.m.
Icterus Index 17.
Icterus Index 8
BEFORE Duodenal Drainage.
AFTER Duodenal Drainage.
I
II
III
IV
V

CHART III

CHART III

TABLE I SUMMARY OF

CASE	SKIN LESION AND DURATION	TYPE OF DYSPEPSIA AND DURATION	LIVER ENLG'D	GALL TRACT TENDER	GRAHAM TEST AND X-RAY	BILIARY TRACT DRAINAGE						GA AN
						SLUGGISH FLOW	PUS	BACT.	BLOOD	EPI-THEL	BILE SALTS	
Mrs. Mc.T. Age 46 No. 3091	Extensive Psoriasis 6+ years	"Biliousness" +Calculi— 20+ years (operated)	+++	++	Large Liver (no G.B.)	Marked Stasis	++	++	+	++	+++	Fre T Ac
Mr. Fr. Age 27 No. 6015	Extensive Psoriasis and Eczema 12+ years	Mild "gassy" "Biliousness" 15+ years	+	+++	G. B. poorly visibilized	Very Tardy Flow	+	+++ Cocci	+++	++	++ Leucin	Fre T Ac
Miss G.B. Age 11 No. 5460	Diffuse Exfoliative Eczematous Dermatitis 6+ years	Mildly "Bilious" 7+ years	+	+++	No Roentgen Study	Marked Stasis	++	+ Cocci	o	++ Liver tube "casts"	++	Fre "Pr
Mrs. M. Age 55 No. 2310	Wide Spread Psoriasis 23+ years	"Biliousness" and "Liver Trouble" (operated) 25+ years	++	+++	Large G.B. C Calculi (Surgical Drainage early)	Marked Hepatic Duct Stasis	++	++ Cocci and Colon B.	o	++	+++	Fre Tot
Mr. A.D. Age 43 No. 8389	Severe "Hives" and "Boils" (?) 2½ years	"Gassy" Dyspepsia and "Bilious" 3+ years	o	++	G.B. Very Poorly Visibilized	Moder-ate Stasis	+	++ Cocci	o	++	o	Fre Tot
Mrs. F.O. Age 43 No. 8049	Acne Rosacea "Eczematous" Stages at Intervals 12+ years	"Liver Trouble" and "Gassy" Dyspepsia— 15+ years	+	++	G.B. Barely Visibilized No Calculi	Marked G.B. and Hepatic Duct Stasis	+	++ Cocci + Colon B.	++	++	+	Fre Tota
Mr. B.C. Age 62 No. 8488	"Hives"— Face and Tongue— Incapacitating Severity On and off— 20 years— Constant 8 months	Irregular Attacks of "Biliousness" for 25 years	+	++	G.B. large and Mottled (Calculi?)	Marked G.B. and Hepatic Duct Stasis	+	o	o	++	++	Fre Tota
Mrs. B.U. Age 40 No. 8974	Generalized Psoriasis— ("Eczematoid" "Weeping") Constant— 1 year	Mild, Irregular "Biliousness" —"Gassy"— Dyspepsia 2 years Skin lesion worse *with* Attacks	+	+	G.B. Poorly Visibilized Liver Enlarged	Stasis + No Liver Fraction	+	o	o	o	+	Free "Pre
Mrs. Gi. Age 40 No. 9272	Eczema— Severe— Ulcerated, Bleeding— especially hands. 2½ years	Slt. "Bilious" 5 years Dyspeptic storms at Pregnancy— at which time skin lesions first appeared	++	+++	Scant Visibiliza-tion G.B. Liver large	Marked Statis G.B. Fraction Scant if any	+	++	o	o	+	Free "Pre

TABLE II SUMMARY OF FI

CASE	PROGRESS OF SKIN LESION	DIGESTIVE STATUS	SIZE OF LIVER	GALL TRACT TENDERNESS	GRAHAM TEST AND X-RAY	GALL TRACT DRAINAGE			
						NO. OF	RATE OF FLOW	PUS	BACT.
Mrs. McI. Age 46 No. 3091	Psoriasis Disappeared after 7" G. T. Dr. *No Recur.* 8 yrs.	Functionally Normal— No Treatment for 7 yrs.	Norm. after 4" G. T. Dr.	None	No Abnormal Capacities	9	Free 600 c.c. last G. T. Dr.	o	o
Mr. Fr. Age 31 No. 6015	Healed in 3 months Slt. Recur. 1½ yr. yielded to treat.	At long Intervals mild "gassy" dyspepsia	Norm. after 2" G. T. Dr.	None	Normal G. B. Shadow	21	Free with "Classical" Sequences	o	Few Cocci
Miss G. B. Age 16 No. 5460	Cleared after Operat. but recurred when Treatment Stopped	Still mildly "Bilious": is treating skin and not systemic ailment	++ also Spleen	+ Common Duct	No Calculi in Ducts Liver ++		Surgical Treatment gave excellent Transient Results: No Treatment of Duct Infection and Liver Stasis allowed		
Mrs. M. Age 59 No. 2310	Marked Benefit after Surg. G. B. Drainage Recurred C Hepatitis	Improved but not Cured. Hepatitis Persisted	+ but Much smaller	+ Common Duct	Hepatic Duct Calculi	6	Treated only rarely— Improved, but never normal liver Fractions		
Mr. A. D. Age 45 No. 8389	Complete Recovery 4 mo. *No Recur.* 1½ yr.	No dyspep. for nearly 2 years	Norm. always	None	Normal G. B. Shadow (Duodenal Adhesion?)	15	Free 300 c.c. last Session	?	Few Cocci
Mrs. Fo. Age 46 No. 8049	Good Result. I—Recur. through Carelessness	Much Improved Infrequent, Mildly "Bilious"	Norm. after 5" G. T. Dr.	Slight +	Still Poorly Filled by Tetra. No Calculi	14	Free 475 c.c. last Sess. Hepatic Fraction +	?	Few Cocci and Colon B.
Mr. B. C. Age 64 No. 8488	Fine Result. No Recur. after 7" G. T. Dr. 1¾ yrs.	Marked Improvement. Only Rare, Mild Attack "Gassy" Dysp.	Norm. after 5" G. T. Dr.	?	Large Atonic G. B.— Calculi(?)	25	Free 1000+ c.c. at times, apparently Hepatic Bile	o	o
Mrs. Bu. Age 41 No. 8974	Good Result but small Patches still Present. Difficult Patient	Improved but mild Hepatitis persists.	Not Palpable	Slight Duct Tenderness	Fair G. B. Shadow— very dense Liver Shadow	20	Fairly Free 165 c.c. last G. T. D. but only scant Liver Fraction.	o	o
Mrs. Gi. Age 40 No. 9272	Striking Impr'v't after 2" G. T. D. Hands Practically normal	No Digestive Disturbance	Norm. after 3rd G. T. Dr.	None	Good Well Formed G. B. Shadow	6	Rapid 375 c.c. last G. T. Dr. Cystic and Hepatic Fr.	?	Few Cocci

OF FINDINGS BEFORE TREATMENT

GASTRIC ANALYSIS	ROSENTHAL	ICTER. INDEX	WIDAL CRISIS	BLOOD NITROG.	BLOOD SUGAR	SENSITIZATION TESTS	BLOOD COUNT				BOWELS			COLON X-RAY
							HGN.	R. B. C.	W. B. C.	EOSINS.	NORM.	COSTIV.	DIARRH.	
Free Hcl. 29 Total Ac. 71	Not Made	Not Obs'd	Not Obs'd	21	130	All Antigens Negative	85%	4,300,000	9,300	1%	o	++	o	Chronic Spastic Colitis
Free Hcl. 40 Total Ac. 62	Not Made	Not Obs'd	Not Obs'd	Not Obs'd	118	All Antigens Negative	75%	4,400,000	8,100	o	o	+	o	Chronic Spastic Colitis
Free Hcl. "Present"	Not Made	Not Obs'd	Not Obs'd	Not Obs'd	Not Obs'd	All Antigens Negative	75%	4,020,000	17,200	8%	o	+	o	Atonic Colon
Free Hcl. 19 Total Ac. 37	Not Made	Not Made	Not Obs'd	18	120	All Antigens Negative	90%	4,100,000	9,000	o	o	++	o	Marked Colon Atony
Free Hcl. 30 Total Ac. 56	18	16	Not Obs'd	21.2	143	All Antigens Negative	75%	4,200,000	7,300	o	o	+	o	Very Spastic Colon
Free Hcl. 12 Total Ac. 24	15	18 / 16	Not Obs'd	14	118	All Antigens Negative	70%	4,700,000	4,700	o	o	++	o	Spastic Colon, Mild Chr. Ulc. Colitis
Free Hcl. 20 Total Ac. 44	50	20 / 16	Highly Suggestive +	17	67	All Antigens Negative	70%	4,200,000	9,600	o	o	+	o	Marked Degree of Atonic Colitis
Free Hcl. "Present"	o to 22	12 to 20	Highly Suggestive +	9	105	All Antigens Negative except Timothy and Goose Feathers	70%	3,900,000	6,400	o	o	++	o	Atonic Colon
Free Hcl. "Present"	30	20 to 15	Highly Suggestive +	16	115	All Antigens Negative	80%	4,200,000	7,600	2	o	+	o	Atony and Dilatation—"Cess-pool" Cecum.

S FINDINGS AFTER TREATMENT

NAGE				ROSENTHAL	ICTER INDEX	WIDAL CRISIS	BLOOD NIT.	BLOOD SUG.	BLOOD COUNT				BOWELS			COLON X-RAY
BACT.	BE.	EPITH.	Bile Salts						HGN.	R.B.C.	W.B.C.	EOSIN.	NORM.	COST.	DIA.	
o	o	+	+	Not Made	Not Obs'd	Not Obs'd	6.3	74	90+	4,800,000	7,400	o	+	o	o	No Objective Anomaly
Few occi	o	o	Few Fragments	Not Made	Not Obs'd	(1) Not Obs'd (2) Positive?	4.2	80	95	5,200,000	6,400	o	+	o	o	No Objective Anomaly
				Not Made	20	Highly Suggestive Positive	Not Obs'd	104	70%	3,390,000	7,650	2%	o	+	o	General Atony
				30	16	Not Obs'd	12	90	85%	4,600,000	6,700	o	o	+	o	General Atony
Few occi	o	o	Scant Debris	10	7	Not Obs'd	2.	84	90%	5,020,000	8,300	o	+	o	o	No Objective Anomaly
Few occi and colon B.	Tr.	+	+	15—20	12—6	Partly Positive	4.2	68	85%	4,800,000	8,600	o	o	+	o	Spastic Descending Colon
o	+	+	Scant Debris	20	8	Not Obs'd	6.1	88	90%	4,700,000	7,400	o	+	o	o	Normal Haustral Markings
o	o	o	Scant	15	9 to 12	Negative Response	4.2	70	85%	4,800,000	8,300	1+	+	o	o	Normal Haustral Markings
Few occi	o	o	+	15	8	Suggestive Negative Response	3.4	82	90%	4,700,000	6,400	o	+	o	o	No Stasis Haustra Appearing

by Campbell and Burgess,[42] Terris and Markinos,[43] Lojander,[44] and by Raymond, LaCroix and Hadida.[45] Our patient returning the highest blood sugar—143 mgm—(Case 8389)—was a 2½ year sufferer from "hives" and "boils," with no liver enlargement, but with tender biliary tract, positive Graham test and moderate biliary stasis at duodenal intubation; his urine constantly was suger free.

"Sensitization Tests" to single or group antigens were performed upon each patient at least once, in some instances several times. Some sixty antigens were employed. In addition, careful enquiry was made into the home life, environment and personal and family habits. We were surprised to note that practically without exception, even in the two instances of urticaria, all evidences of what is loosely styled "allergy" were lacking. In case 8974, mild, positive, responses were shown to timothy and goose-feathers, but nothing in the history suggesting that these agents were factors in causing or maintaining the dermatoses was obtainable. Our experience with "sensitization tests," together with other observations upon the patients comprising this group, supports the position of Engman and Weiss,[46] Barber,[47] Ferris,[48] of Larat and Siebenman,[31] Menagh[13] and of Galloway,[30] namely, that when what we call an inherited "predisposition to hypersensitiveness" is present in the individual (a condition existing in 10-15% of the human family according to Duke),[6] many substances occurring in an abnormally functioning digestive tract fail to complete the cycle of normal digestion and gain entrance to the general circulation. Attempts at the completion of this metabolic cycle of these substances by the blood results in transient or constant skin anomalies of a circulatory type and are often accompanied by dermatoses. It follows that patients may be "sensitized" to single or many substances, yet give negative *"antigen"* responses, partly because the skin and body fluids are, from time to time, in a "refractory phase" or because numerous substances, acting at the same time, prohibit definite, individual allergic responses.

Opie[14] has emphasized the organic damage which proteins and other toxic substances introduced into the general circulation produce in the liver. Egg white introduced into the veins of rabbits appears in the urine in one-half hour, whereas if it be injected into the mesenteric vein, its appearance in the urine is greatly delayed or does not occur. Opie states that thus the liver serves as a buffer to protect the body from material that may find harmful entrance by way of the gastro-intestinal tract. Even if animals are sensitized, if the liver be intact, it may inhibit protein intoxication by "fixing", through the peculiar endothelium of its sinusoids, substances dissolved in plasma. But, if the process is long maintained, this "buffer" function of the liver results in the "fixed" substances causing definite organic damage and diminished function of the viscus itself.

Blood counts—Before treatment for the series, the hemoglobin averaged 78%; erythrocytes, 4,200,000 and the leucocytes, 8,500.

Differential formulae were normal with one exception, Case No. 5460—

the child, where 8% eosinophilia was recorded. In view of the absence of eosinophilia in the other patients, it was not possible to attribute this relatively high eosinophile percentage to the co-existing eczema, as some writers have reported (Hazen). [48] This patient's stools were free from parasites, and there was no associated asthma.

Colon Roentgenograms following barium enemata were, in all instances abnormal. In five patients, atony, with general or local (cecal) retention was pronounced. The remaining four subjects exhibited so called "spastic" colons; in one patient (Case No. 8049) mild, chronic ulcerative colitis was demonstrated. Certainly, these observations would seem to support the generally held opinion that in chronic dermatoses, the colon may be a locus in which noxious substances may be elaborated and then may pass to the liver as potentially harmful agents.

Management

(a) *Preliminary Survey* The sequence of events already detailed with respect to our first patient affected with hepatitis and psoriasis (Case No. 3091) nearly nine years ago, largely guided us in the treatment of the group of dermatoses here reported. We could not convince ourselves that, with the return of a huge liver to normal size and restoration of digestive function, the concomitant complete cure of an extensive psoriasis of long duration was a coincidence. Particularly so, when objectively, duodenal intubation blood chemistry and roentgenologic study presented evidences that, with the cure of the psoriasis, liver function definitely had been changed for the better.

For such few subjects exhibiting dermatoses as come into our practice, we planned deliberately a mode of management which included as treatment of the skin lesions only measures concerned with keeping them clean and protected, but which had for its major purpose restoration of liver and alimentary tract function.

In summary, our handling of patients of this class follows:

1. History, emphasizing not so much the dermatologic classification of the lesions, but determining by enquiry and laboratory study of the skin pathology whether or no we are dealing with a lesion of "extrinsic" or "intrinsic" etiology; if the latter, what, if any, has been the digestive life of the subject. We do not concern ourselves with dermatoses of "extrinsic" cause; they are the exclusive property of the dermatologist.

2. Physical examination from head to foot, paying particular attention to condition of the mouth, throat, abdomen, rectum and lower colon.

Photographs of the skin lesions and, when possible, their proper placement so far as nomenclature is concerned by a skilled dermatologist.

3. Complete blood study, including Wassermann and Kahn tests, differential and blood platelet counts, coagulation time, blood chemistry.

4. "Sensitization" tests.

5. Stool, urine, and gastric test meals.

6. Diagnostic duodenal intubations.

7. Rosenthal test, icterus index, and Widal "crisis."

8. Gastrointestinal roentgen observations including Graham routine.

(b) *Therapy* When the diagnostic survey has exhibited evidences that, associated with a dermatosis, functional liver deficiency exists, the patient is considered from the viewpoint of whether surgical or non-surgical measures shall be applied as the better aid to restoring hepatic activity. If our diagnostic survey indicates the presence of biliary tract calculi or an infectious process of actual or impending acuteness, provided there are no contraindications (cardiac dysfunction, malnutrition, hypertension, etc.) surgery is advised as the first step toward relieving a damaged liver. Cholecystostomy, with long-continued drainage of hepatic ducts, certainly is to be prefered over cholecystectomy; the latter operation is of relatively little value apart from the possibility of anticipating acute crises; there is no valid reason for treating a part of the ailment when one is able to attempt relief of the whole.

Cases Nos. 3091 and 5460 (Table II) demonstrate how but partial or temporary improvement in liver function—with associated limited relief of dermatoses—follows cholecystectomy. In both these patients, residual and, potentially far more serious anomalies involved the liver than its excretory passages at the time of operation. Case 3091 developed psoriasis subsequent to cholecystectomy and, as enlargement of the viscus progressed, skin lesions became aggravated. Not until drainage of the hepatic duct radicles by duodenal intubation became possible, was there relief of the digestive disturbance or the dermatosis.

Case 5460—the young girl—was subjected to what amounted to an emergency cholecystectomy: within a few weeks hepatic enlargement disappeared and there was striking alleviation of the dermatosis. However, hepatitis still remained and became more extensive. Duodenal intubation was neglected, with the consequence that liver (and later spleen) enlargement again occurred—(really, a cirrhosis of the type produced experimentally by Rous and his co-workers and, more recently emphasized by Stengel and Pratt), accompanied by recrudescence, milder, to be sure, of the exfoliative dermatosis. The lesson carried by the course of these two cases is evident and is significant relative to management.

Case 2310, with a liver type of indigestion for longer than 25 years and psoriasis for about 23 years, experienced marked alleviation of both dyspepsia and skin affection, subsequent to cholecystostomy performed seven years after indigestion appeared. How long surgical drainage was persisted in was not stated, but proof that duct infection and hepatitis remained was furnished by our demonstrating calculi in the gall-bladder remnant and in the hepatic ducts at the time of our first study. Enlarged liver, duodenal intubation returns and greater than normal blood nitrogen and sugar values, indicated persistence of hepatic dysfunction; the dermatosis was only partially alleviated by a second operation, by six duodenal intubations (never satisfactory and carried out at long intervals), diet and medicines. The blood nitrogen and sugar values

approached normal, but relatively long Rosenthal dye retention and high icterus index suggested permanently hampered hepatic activity as a factor in maintaining some degree of dermatosis. Recurrent "bilious" storms were invariably accompanied by recrudescences of the skin lesion.

Seven of our patients were managed non-surgically; one (Case 8488) not by choice, inasmuch as history, Graham test and duodenal intubation strongly indicated the presence of gall-bladder calculi, but because cardiac damage and general arteriosclerosis imposed a serious operative hazard.

Treatment comprised a diet low in protein and fat (particularly concentrated proteins and animal fats), frequent and carefully supervised duodenal intubations, adequate doses of ox gall (30 to 90 grains daily, and administered before food intake), intestinal eliminants (calomel, with subsequent saline catharsis) in the instances of colon atony and less drastic purges, as cascara and senna or one of the mineral oil preparations when colon films demonstrated spasticity, and, in selected instances, the internal exhibition of sodium salicylate.

Diets of limited protein and fat intake were selected with the object of physiologically saving the liver. Attempts were made to balance the diets and to exhibit adequate vitamins. Such diet is well tolerated by even damaged livers. The investigations of Moise and Smith,[49] dealing with the effects of diet upon tissue growth and repair in livers subjected to standard, severe tissue destruction by chloroform injections, suggests that our dietaries are potentially beneficial to a degree greater than are any known medicinal agents.

EFFECTS OF TREATMENT UPON THE DERMATOSES (TABLE II) Five of our seven patients, non-surgically managed, had entire disappearance of their skin lesions (psoriasis 3 cases; urticaria 2 cases). These patients have had no recurrence of their dermatoses over an average time of approximately 3½ years (individual range of ½ to 9 years). Previous to treatment their dermatoses had existed practically constantly for an average time of 9 years. These patients all permitted thorough management along the lines above summarized and were under treatment approximately six months. Improvement to a degree called "cure" by the patient was strikingly prompt in several instances (Cases No. 8389, 8488 and 9272), but, in the presence of physical and laboratory evidences of hepatic dysfunction, continued treatment was carried on.

The importance of patience and persistence cannot be emphasized too strongly; patients are apt to "slack" when their skins again become presentable and itching and burning are no longer annoying. Then the continued management becomes most difficult. Irrespective of the favorable progress of the dermal lesions, it is our practice to insist on strict adherence to the therapeutic plan instituted until, symptomatically, physically, roentgenologically, by duodenal intubation, dye tests, icterus index, blood chemistry and, in certain cases, Widal "crisis," objective evidence is presented that the goal set in exhibiting our

therapeutic regime, namely, restoration of liver and biliary tract function, has as far as possible, been reached. In this series, of the seven non-surgically managed patients, the two patients in whom we obtained the least satisfactory results (Cases Nos. 8049 and 8974) were those who lacked persistence and patience and who, when alleviation satisfactory to *them* but not to *us*, had been secured, either stopped treatment or carried it out in haphazard fashion.

Proof that Treatment Favorably Affected Liver and Biliary Tract Digestive Function: Table II, compared and contrasted with Table I, taken in association with the case summaries submitted, records our experience. Six of our nine patients consider themselves free from dyspepsia of "bilious" nature; all improved, but careful analyses of their digestive lives indicate that some degree of liver damage, with slight imperfection in function, still persists. However, none of the patients is in any way a dyspeptic invalid, but all are active in home, social or business life.

Liver Enlargement has persisted in only two instances (Cases No. 5460 and 2310). Neither of these patients was adequately treated or, perhaps, treatment was instituted too late to achieve the optimum result. Five of the patients were normal to palpation over the biliary tract; two still exhibit slight degrees of tenderness and two (those incompletely managed) are definitely tender to moderate pressure.

Roentgenologically, hepatic duct or gall bladder calculi can be shown in two patients; gall-bladder visualization by Graham's test is now normal in four cases, while in two, fair to poor shadows are seen.

Duodenal Intubation: The average number of "drainages" for the series (omitting Case No. 5460) was approximately 15—an individual range of from 6 to 25. These figures sufficiently indicate the persistence required in order to obtain good results. Particularly, when hepatitis is of advanced degree (e.g. Cases Nos. 8488 and 8974) are many duodenal intubations, and at short intervals, needed. Carried on according to such plan, it is surprising how, from a patient, who, at first examination, yielded bile admixtures so scant as to make analysis difficult, large volumes of hepatic duct bile (in excess of 1000 c.c. in Case No. 8488), normal in character, eventually are obtained; and with this accomplishment, liver size decreases, dyspepsia disappears and skin lesions subside.

Rosenthal Tests showed but irregular returns before and after management, except in two instances (Cases 8488 and 9272) where dye retention time was reduced respectively from 50 to 20 and 30 to 15.

The Icterus Index in five patients studied before and after management was noticeably lower; pretreatment average was 16.8 and post-treatment average was 8.6—a figure well within normal range.

Widal Crisis could be compared before and after treatment in but two patients (Table II). Charts 1 and 2 would appear to indicate that, insofar as restoration of a liver "barrier" function against noxious substances carried to it via the portal vein is con-

cerned, management had been beneficial.

Blood Nitrogen figures were uniformly lower after treatment. For the series, the average was 5.3 as against an average of 17 before treatment. Two instances of hepatitis (Cases No's 2310 and 8488) still carried rather high figures: 12 and 6.1 respectively.

Blood Sugar averaged, in 8 comparable patients, approximately 80 after treatment in contrast to 113 before. There was a reduction in all patients, except Case No. 8488 (urticaria with hepatitis and gall-bladder calculi).

The Blood Picture exhibited improvement in all patients except Case No. 5460, the child, where in association with progressive liver cirrhosis, splenic enlargement with a suspicion of an impending Banti's syndrome has developed.

Colon Roentgenograms suggest restoration of normal bowel function in six of the nine patients. These observations are in accord with the clinical observation of normal evacuations. Three patients (Cases Nos. 5460, 2310 and 8049) still experience constipation; their colon films exhibit atony or spasticity and one case chronic ulcerative colitis.

Discussion and Summary

A group of nine patients, exhibiting chronic, endogenous skin affections, was likewise found to experience digestive dysfunction of the type commonly associated, clinically, with inflammatory lesions of the liver and biliary tract.

The nature and the degree of the digestive dysfunction, was clinically summarized in each patient, before and after treatment, by physical and roentgenoscopic examinations and by studies of objective evidence secured by duodenal intubation; before treatment, definite proof of liver and biliary tract disease, was established for the group.

Evidence is presented apparently indicating that in this group of endogenous skin lesions, before treatment, at certain stages, the blood serum contains increased quantities of urea nitrogen and glucose.

Functional tests to determine the excretory capacity of the liver to a test dye, before treatment, indicate moderate retention. Such retention similarly is shown by relatively high icterus indices.

When estimated, the "protective" or "barrier" function of the liver in this group of cases, as determined by Widal's "hemoclastic crisis," appears to be reduced.

"Sensitization" or "allergic" phenomena toward numerous antigens were not exhibited by this group of patients.

Evidence is adduced suggesting that in certain endogenous and chronic dermatoses (clinically called "eczema", "hives", "urticaria", "angioneurotic edema", "psoriasis") chronic inflammatory lesions of the liver and biliary tract prevent normal excretion of bile and limit the storage of glycogen and, consequent upon the resulting reduction of the "barrier" function of the liver, permit toxic substances (proteins, polypeptids, or their derivatives)

to pass into the blood stream in greater than normal quantity. It is suggested that this constant or intermittent increase of toxic substances in the blood stream interferes with normal mechanical and chemical conditions in the capillary bed. Depending upon the nature of the toxic substances and the tissue response to such, (primarily a conservative process) dermatologic lesions follow. They differ in picture, kind and degree since they are dependent upon the local tissue response (usually skin elements and neurologic structures) to the circulating toxin.

Chronicity of the lesions depends upon the constancy or irregularity of the hepatic and biliary tract defect, the nature and quantity of the toxic protein derivative in the capillary bed, and the local resistance (congenital or acquired) of the skin structures. Dyspeptic storms (commonly called "bilious attacks") precede or accompany the initiation or the recrudescences of the dermatoses. The continuance of the lesions would seem, primarily, to be dependent upon the toxin-with-tissue reaction in an area of skin by the affected capillaries and arterioles and, secondarily, upon the dermal deformity consequent upon attempts at repair, aggravated or not, by external traumata.

A plan for the examination of patients affected with endogenous dermatoses, with or without dyspeptic syndromes, is detailed.

A method of management for patients falling into the above classification is detailed. In principle, it includes no local treatment of the dermatologic lesions other than cleansing and mechanical protection, but, by suitable diet and attempts at promoting free excretion of bile and preventing hepatic and gall tract stagnation, has as its purpose, the restoration of normal, physiologic, hepatic function: protective, storage and the elaboration and excretion of bile.

Observations presented upon nine patients who were treated in line with this principle seemingly demonstrate that, when normal hepatic and biliary tract function was obtained, (as shown clinically, roentgenologically, by duodenal siphonage, and serologic studies), the dermatoses disappeared or became less pronounced. When hepatic function did not approach normal, dermatoses recurred or persisted.

Study of this group of patients affected with endogenous dermatoses suggests that the hope of relief or cure of what previously have been regarded as incurable lesions lies, not in elaboration of measures to combat the local skin damage, but in attacking the problem from the "systemic" aspect. Investigations directed in such lines, will, not infrequently, disclose faulty hepatic function, attempts at relief of which, will be followed by improvement, often striking in rapidity and extent, of the dermatoses.

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The Pathology of the Nodular Goiter*

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A DECADE ago it commonly was thought that the anatomical examination of thyroids removed from patients suffering from hyperthyroidism did not reveal changes which could be correlated with the clinical findings. Consequently, many classifications of diseases of the thyroid gland were proposed, based largely either upon clinical features or on anatomical changes. Such classifications were very simple or very complicated, and often confusing. In the main, the proponents of these classifications might be grouped into those who differentiated between two types of hyperthyroidism and those who maintained that such differentiation was not justified and could not be substantiated.

The type of hyperthyroidism which has given rise to much controversy is that which is associated with the so-called toxic adenoma. It is this phase of the pathology of the thyroid that will be discussed, in an effort to determine the significance of nodules in the thyroid, the nature of true adenomas of the thyroid, and the relationship between the anatomical changes and the clinical findings. Two terms need strict definition, for it appears to me that much of the confusion has resulted from the loose application of terms and a faulty conception of what constitutes an adenoma and what constitutes hyperplasia.

The term "adenoma" implies a new growth of epithelial tissue of a glandular nature. In other words, an adenoma is an epithelial, glandular tumor, the cells of which are arranged atypically and yet resemble those of the organ from which they are derived, and the tumor grows at the expense of the organ, without subserving any useful function. In order to strengthen the evidence that the great majority of nodules in the thyroid are not true adenomas in this sense, considerable time might well be spent on the origin of adenomas wherever they may be, but this short definition must suffice. A similar change of opinion has taken place with regard to nodules in the prostate and breast.

The other term that requires just as strict a definition is "hyperplasia." Hyperplasia means an increase in the bulk of the tissue due to the increase in number of its elements or cells. It is nearly always associated at some time or other with simple hypertrophy, which is an increase in the size of the elements or cells. Furthermore, this term implies a direct re-

*Based on a paper read before the Milwaukee Academy of Medicine, January, 1929.

lationship between this anatomical change and the function of the organ.

Another fundamental fact must be stressed here. The histological changes observed must be considered as episodes in a cycle of events. The variations from the normal do not of themselves constitute independent and complete lesions, and do not signify a finite change or the end result of a limited process. Careful attention should be given in order to differentiate and separate accidental and secondary changes, which may be extensive enough to color and obscure the fundamental pathology. These changes are generally those of degeneration and will be referred to below.

The subject of adenoma of the thyroid is by no means of anatomical interest only, for a step in the right direction will be made when these tumefactions are brought into direct relationship with the pathological physiology of the gland. If this can be done, confusing classifications may be dispensed with. Just when the term adenoma was first applied to the nodular thyroid is obscure. At any rate, it does seem that the term was applied on the basis of certain gross appearances, and not primarily upon the histology. Thus, the sharp demarcation of these nodules from the surrounding tissue and their striking gross differences impressed the observers. The histological findings were then attuned to the gross diagnosis. Thus resulted the colloid adenoma, cystic adenoma, calcified adenoma, etc.

The theory has been advanced that these nodules are not adenomas as the term has been defined here, but are the result of phases of activity and remission in the gland, and the only tumors deserving the name adenoma are those which are called fetal adenomas. These so-called fetal adenomas are not altogether uniform in appearance, nor shall it be taken for granted that these tumors have been proved to arise from fetal cells. I have paid particular attention, in examining thyroid tissue, to finding fetal rests or fetal cells, as Wolfler[1] described them, and from which it has been presumed that fetal adenomas take origin. I have never satisfied myself that these rests exist or can be recognized. All atypical groups of cells could be explained satisfactorily by serial section and by their morphology to be parts of acini in various stages of distention. It does seem that the existence of "Wolfer's rests" has been too easily accepted. Rienhoff[2] has also failed to find any such areas by methods of micro-dissection and reconstruction. The majority of fetal adenomas are encapsulated. Occasionally very small ones are not. They may be multiple. They are easy to recognize, consisting of anastomosing cords of cells separated by sinuses. Colloid is absent or very scanty and thin. Very occasional early follicle formation may be noted.

More significant are the so-called toxic adenomas. These include the various forms of degenerative changes noted above, as well as very compact cellular tumors. The latter are localized areas of hyperplasia, and are usually of microscopic size, but may be visualized by the naked eye.

The term adenoma crept into the literature of the thyroid, and by an easy method of adoption became an accepted fact. That these adenomas

could become toxic was as easy to adopt. The main advocate of the toxic adenoma in this country is the Mayo school, headed by Plummer. If one subjects their evidence to critical analysis, it is apparent that the distinction between a thyroid with toxic adenoma and hyperthyroidism or exophthalmic goiter is not based on indisputable findings. Plummer[3] has come to the conclusion, as a result of a study of clinical findings in a large number of cases of goiter examined at the Mayo Clinic, that there are two distinct types of hyperthyroidism, each associated with distinct pathological changes in the thyroid gland; that in one type the hyperthyroidism associated with the clinical syndrome of true exophthalmic goiter is always accompanied by hypertrophy and hyperplasia of the thyroid gland, and that in the other type hyperthyroidism is not associated with hypertrophy or hyperplasia, but with the occurrence of adenomas; and that the symptoms are due to adenomas and are distinguishable from those occurring in the exophthalmic goiter. Nevertheless, Boothby[4] quotes Wilson and others as being unable to find any constant pathological differences in the adenomas that produce symptoms of hyperthyroidism and those that do not produce symptoms of hyperthroidism. Graham and Cutler[5] writing of the administration of iodine, state that they have been unable to recognize any clinical or pathological difference of sufficient fundamental significance between these types of thyroids to establish them as distinctive diseases. In other words, in two cases of toxic goiter with symptoms and signs quite similar, the one without nodules is diagnosed as exophthalmic goiter and the nodular one as toxic adenoma. Dunhill[6] believes that the differences are those of degree and not of kind. There is no *single symptom* or *group of symptoms* pathognomonic for exophthalmic goiter as opposed to the so-called toxic adenoma. Likewise, there has been failure to recognize a single anatomical or histological alteration in the thyroid in either the adenomatous or nonadenomatous portion of the gland that is necessarily pathognomonic for exophthalmic goiter as opposed to toxic adenoma. There is sufficient clinical data proving that iodine produces a temporary remission in all types of hyperthyroidism. It is probable, therefore, that there is a similarity of essential pathology in all varieties. From this standpoint, clinical and histological examinations are ample now to show that there is no qualitative difference between the mechanisms produced by hyperthyroidism in adenomatous goiter and in exophthalmic goiter. If it were true that an essential difference exists between the two types, it might be expected that one of these might be resistant to iodine. The reverse is true. No single type is alone resistant.

Rienhoff and Lewis,[7] in writing of the relation of hyperthyroidism to benign tumors of the thyroid, present strong evidence in favor of the theory that these so-called adenomas are not true neoplasms. In their opinion, the terms "toxic adenoma" and "hyperfunctioning adenomatous goiter" are misleading and incorrect. Reinhoff[8] had previously shown, in seven cases of hyperplasia of the thyroid, studied before and after the administration of

iodine, that the iodine involution brings about a reversion to the colloid state. Rienhoff and Lewis now demonstrate that in about 92% of cases colloid involution progresses to the point where a nodular thyroid results. These nodules are not neoplasms, but are rather involutionary bodies, and the regressive results of previous hypertrophy and hyperplasia. In any nodular goiter the number and size of these nodules are dependent on the chronicity, the severity, and the number of remissions in the course of the disease. Moreover, the hypertrophy and hyperplasia may be confined to certain areas in the thyroid gland, so that after repeated cycles of activity and remission, localized and encapsulated nodules develop. The capsules result from the pressure atrophy on the surrounding more or less inactive gland. The clinical picture of these cases of nodular goiter is merely an attenuated one of that seen in the typical exophthalmic goiter. The histological picture of these nodules does not conform with that of the recognized tumors of the thyroid, but rather retains the microscopic appearance of hypertrophy and hyperplasia. Rienhoff and Lewis were unable to show that the presence of a benign neoplasm was the cause of hyperactivity of the gland or of toxic manifestations, for in those cases diffuse involvement around and away from the tumor was demonstrated. Furthermore, they could find no proof that benign tumors of the thyroid can give rise to toxic manifestations by virtue of a peculiar secretion. They recommend that the following terminology be used: "Nodular goiter, with or without hyperthyroidism," and "diffuse goiter, with or without hyperthroidism."

Hertzler[9] considers that the various forms of goiter and hyperthyroidism are stages in a long-continued disease process, and asserts that in these nodular goiters new alveoli arise from the interstitial cells. The presence of interstitial cells has never been proved to my satisfaction. Thomas[10] carefully studied 32 cases of nodular goiter, all presenting the clinical symptoms of hyperthyroidism. Sections revealed hypertrophy and hyperplasia. He could trace a close parallelism between the degree of morphological change and the severity of the symptoms. The only difference between these nodular goiters and exophthalmic goiter seems to be one of degree.

When a large number of exophthalmic goiters is studied, one finds only a narrow dividing line between the toxic adenoma and the exophthalmic goiter. In most cases, if one studies the life history of the patient carefully, the toxic type is an acute exacerbation of the chronic state rather than a new or distinct process. The toxic stage is always associated with hyperplasia, and so-called exophthalmic goiter differs from the so-called toxic adenoma merely in degree. In my own experience, I have never met with a nodule showing no hyperplasia removed from a patient with definite symptoms of hyperthyroidism without being able to demonstrate hyperplasia elsewhere in the gland. If hyperthyroidism is present, the sections of the gland will reveal evidences of hyperplasia. In nodular goiters the hyperplasia is generally in the non-nodular portion, although the nodules may occasionally

contain hyperplastic epithelium. The degree of hyperplasia present will depend upon the severity of the disease, its chronicity and whether or not the patient had been treated with iodine. Most of the nodules that attain an appreciable size are hyperinvoluted areas filled with colloid, although in these nodules one frequently finds residual manifestations of hyperplasia as demonstrated by the columnar epithelium and intra-acinar proliferations.

Ginsburg[11] recognizes the toxic adenoma as a clinical pathological concept, yet fails to observe any fundamental distinction between toxic adenoma and exophthalmic goiter except as the variations of a single disease. He accepts the nodules as being true adenomas, which would imply that the adenomas react in exactly the same way as the non-adenomatous portion of the gland. How much more logical it is to consider these nodules as resulting from involution. The structure of these nodules does not differ fundamentally from that in the non-nodular portions of the gland. Aschoff[12] believes that these nodules are true adenomas and may give rise to symptoms of hyperthyroidism. The latter statement is true, inasmuch as hyperplasia may recur in involuted areas, but that very fact would seem to be evidence against these nodules being neoplasms.

Marine[13] has firmly established that the thyroid gland undergoes a definite cycle of cell changes in response to stimulus. These changes are hypertrophy and hyperplasia, and reversion to the colloid state. We have modified Marine's schematic representation of thyroid activity and have outlined its phases in Chart I. The chart is self-explanatory and indicates the repetitions and cycles of the gland and the likelihood of the occurrence of secondary changes.

There is only one morphological

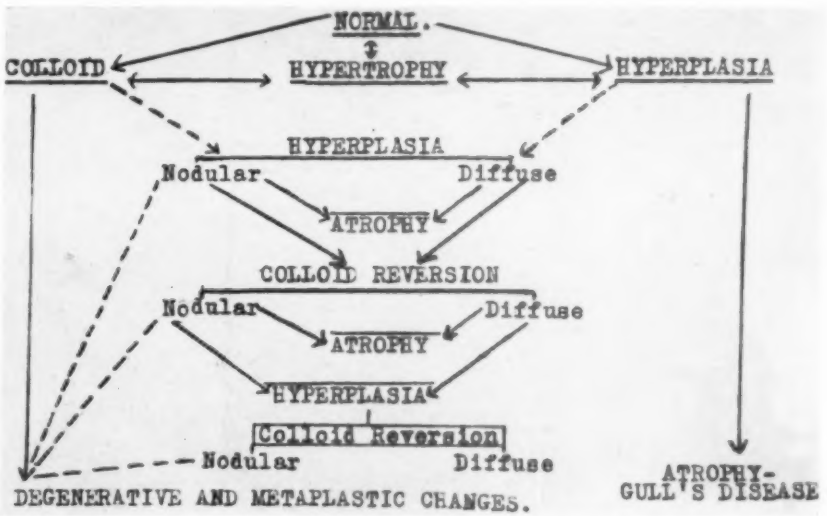

CHART I

cycle through which the thyroid may pass, regardless of the activating stimulus. First, the gland responds by increased activity and later by increased size, and reverts to the resting colloid state when the stimulus has subsided.

Marine has persistently maintained and demonstrated that there is no sharp line of demarcation between diffuse hyperplasia and adenoma. Wegelin[14] has demonstrated the same cycle of nodule formation in rats, and showed that these arise from adult regenerated epithelium. Kline[15] came to a similar conclusion from his study of goiter in man. Clinically and anatomically, all toxic goiters, like all simple goiters, whether diffuse or nodular, are of the same disease process, different only in degree and duration, and in the cycle in which they happen to present themselves. The hyperplasia in adenoma is not different from that in exophthalmic goiter, and, moreover, both revert to the colloid state in exactly the same manner and under the same influence. In the past four years I have studied over 500 specimens, and basing my interpretation on the principles outlined here, have been able to correlate satisfactorily the histology

Fig. 1. Fetal Adenoma.

with the clinical history. The examination of the gland also explains and records the effect of iodine therapy.

It must be admitted that insofar as the etiology is concerned, very little is known. Statistics[16] indicate that low iodine intake is correlated with simple goiter and exophthalmic goiter. More complete surveys of the incidence of hyperthyroidism with nodular and nonnodular goiter and the geographic distribution of "low-iodine areas" will be of interest. Kunde[17] has succeeded in producing the features of exophthalmic goiter with exophthalmos through the administration of thyrotoxin.

Much has been said of the constitutional diathesis in hyperthyroidism. A constitutional peculiarity, predisposition or diathesis does not constitute a disease. Even if a predisposition exists, it merely renders a patient susceptible to an etiological or exciting agent. In the case of hyperthyroidism there are at present two schools of thought. One school, while admitting that the thyroid gland plays an important rôle in the symptomatology of the disease, is, however, impressed with the fact that we must look beyond this gland for the primary essential lesion. In support of this position there is cited

FIG. 2. Localized Hyperplasia in Nodular Goiter.

evidence that not only is the thyroid abnormal, but the lymphoid tissues, thymus, and adrenals are always involved in an important way. Thus, they maintain that hyperthyroidism is really secondary. Warthin,[18] in presenting his views on this point, states that toxic adenoma and exophthalmic goiter possess the same pathologic entity. I cannot accept Dr. Warthin's statement that we possess no histological criteria so far as the thyroid epithelium is concerned. In my experience, the changes in the epithelium are more striking and constant than the presence of lymphoid tissue. Hyperplasia of some degree is a constant finding in hyperthyroidism. The changes in the thymico-lymphatic apparatus as described by Dr. Warthin and others are too often overlooked. Whatever the relationship between the lymphatic system and the thyroid, the fact that these systemic changes are present with nodular and non-nodular goiters in hyperthyroidism is additional proof that these manifestations in the thyroid gland are not indicative of distinct and separate disease processes.

Clinical experience is to the effect that the great majority of these patients are relieved when the mass of thyroid

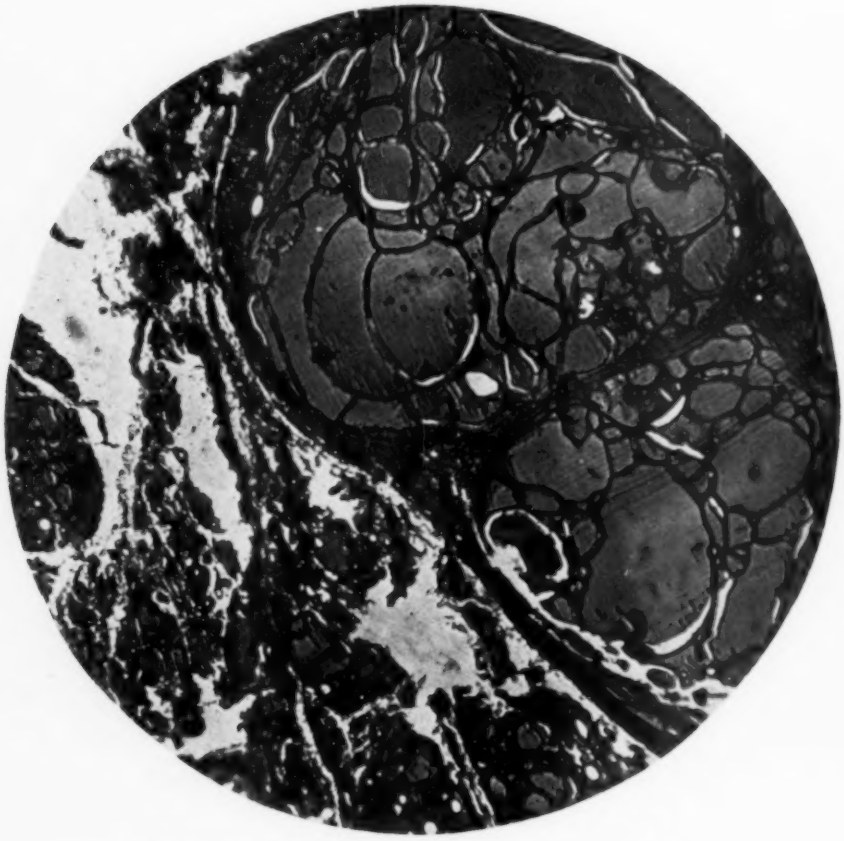

FIG. 3. Localized Colloid Reversion in Nodular Goiter.

is reduced surgically or reverted to the colloid stage, and to get permanent clinical improvement in the presence of persistent hyperplasia of the thyroid is unknown. Whatever the etiology may be, the disease is manifested through the thyroid gland. There is hardly any doubt but that in years to come fundamental facts will be uncovered which will render many of the hypotheses, and consequently much of the treatment of this disease antiquated, and it is not at all unlikely that surgery of this gland for hyperthyroidism will become obsolete. At present subtotal thyroidectomy is performed both for nodular and for non-nodular types.

To invest the thyroid with dysfunction and hyperfunction is harmless, provided the two terms are used interchangeably, but to maintain that these represent different diseases and account for different disease pictures, real or fancied, is at present without foundation. To me the differences, clinically and anatomically, are such as can be explained on the basis of duration, severity, and constitutional susceptibility. Not all people respond alike to intoxicants.

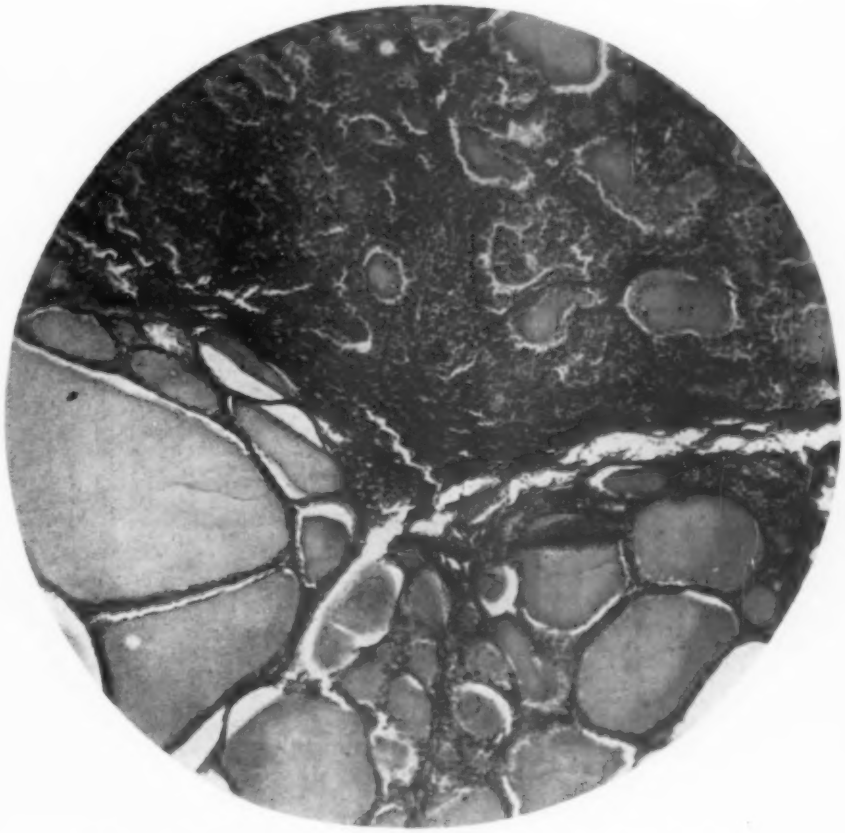

FIG. 4. Hyperplasia and Colloid Reversion in Nodular Goiter.

There is no sign or symptom pathognomonic of toxic adenoma or of Graves' disease. At the present time it is impossible to make a differential clinical diagnosis between a true benign neoplasm, hyperinvoluted nodule, and a tumor resulting from localized hypertrophy and hyperplasia in a patient with hyperthyroidism. Nodular and diffuse goiter, with or without hyperthyroidism, is an adequate clinical classification. Pathologically, one may classify them as "nodular goiters with areas of hyperplasia," or "diffuse colloid goiter with focal areas of hyperplasia," or "diffuse hyperplasia with colloid reversion," depending upon the quantitative relationship between the colloid content and the hyperplastic areas. Parenchymatous or fetal adenomas are separate entities. These tumors possess a characteristic histological structure, and have never been proved to be the cause of hyperthyroidism, nor do they offer any evidence of undergoing cell changes which have been shown to be associated with this clinical syndrome.

In reviewing the literature of the thyroid, one is struck with the mass of opinion and of theory, all presenting a maze difficult to understand and to

FIG. 5. Encapsulated, Hyperinvoluted Nodule and Resting Thyroid.

correlate with such fundamental facts as have been established. Words have been used to connote a concept, and then it has been taken for granted that this concept is a reality. The literature of the thyroid deserves a careful, systematic house-cleaning. Only a small portion of the literature is truly valuable. How long this will remain valuable is for the future to tell us. There is no proof that hyperplasia is either the result or the cause of the train of symptoms we call hyperthyroidism. We know only that it is associated with it. There is also no proof of the toxicity of "adenomas." "Toxic adenomas" are best understood when considered a part of the cycle of activity exhibited by the thyroid in response to unknown stimuli. There is no reason at present to believe that the etiological factors in nodular and nonnodular goiter differ in kind. They may differ in degree.

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A Case of Acute Leukemia With Unusual Cell Forms in the Blood

By Harold Bowcock, M.D., and Everett L. Bishop, M.D., *Pathologist to the Steiner Clinic, Atlanta, Ga.*

THE syndrome designated as acute leukemia is attracting increasing interest. Recent reports have been characterized by extreme caution in classifying an acute leukemic reaction as either lymphoblastic or myeloblastic in type. Minot[1] emphasizes the fact that it is impossible to always classify individual cell forms and that it is more important to recognize that a cell type is: 1, normal and mature; 2, abnormal and mature; 3, normal and immature; or 4, abnormal and immature. Clough and Piney[2] describe the usual morphological differences between the lymphoblast and the myeloblast, but the impossibility of differentiation between such cells is readily appreciated after a study of the illustrations of cell forms from cases of acute lymphoid and myeloid leukemia appearing in Cowdry's Special Cytology.[3] Recent reports by Sabin, Austrian, Cunningham and Doan,[4] and Wilson and Cunningham[5] of supra-vital studies of living cells in subacute myeloblastic leukemia and acute lymphatic leukemia, respectively, suggest a new method of morphological study which may prove to be of differential diagnostic value. Each group of authors had the opportunity of studying only one case by the method of supra-vital staining, but Wilson and Cunningham were able to demonstrate differences between the cell type of their case and that of Sabin, et al.

Even a correct diagnosis of acute leukemia presents difficulties from the combined viewpoint of the clinical picture and the blood picture. The differential points have been considered in some detail in the reports of Schenck and Pepper,[6] Krumbhaar,[7] and Crawford and Weiss,[8] illustrated by case reports.

Warren[9] and others emphasize the fact that it is of no practical importance to differentiate between the types of acute leukemia as all are uniformly fatal within a short period of time. Warren has investigated the available world literature of the subject and has reviewed 85 autopsied cases to which he has added the data from 28 unreported autopsied cases. Of the 113 cases studied, he found the following age incidence: Under 10 years of age, 24 per cent; between 25 and 35 years of age, 42 per cent; between 45 and 50 years of age, 20 per cent. Males were affected throughout in a proportion of 2 to 1, but at the menopause age the ratio was reversed with almost 3 females to 1 male. He found

that the myeloid type of leukemia was more common than the lymphoid. A duration of the disease of 6 months was arbitrarily chosen for the designation acute, but death occurred within 8 weeks of the onset of symptoms in 84 per cent.

The following case showed many interesting and unusual features. A presumptive diagnosis of acute lymphoid leukemia was made in this instance, although it is realized that this designation may be incorrect and that the characteristic abnormal cell may have been myeloid in origin. Supra-vital studies of the blood were not made, but in fixed preparations the characteristic immature cells of our case showed a marked resemblance to the cells seen in a fixed preparation kindly loaned to us by Dr. Cunningham and obtained from the case reported by Wilson and Cunningham.

The debated question of etiology will not be considered beyond the mention of the following facts. A neoplastic etiology has been considered by many authors, (Warthin) and Sabin et al and Wilson and Cunningham have often observed amitotic division occurring in their supra-vital preparations. One case showed many mitotic figures in the blood and a smaller number of cells, the nuclei of which we believed to be undergoing amitotic division. other hand, our case had an onset with a clinical picture resembling a respiratory infection.

CASE REPORT: Mrs. A., aged 43, was admitted to the hospital for examination March 18, 1929. The complaints were weakness, sore throat, cough, afternoon elevation of temperature, night sweats, nausea and vomiting.

The family history was unimportant.

The patient had had the usual diseases of childhood, with uneventful recoveries. At the age of 13 she had had uncomplicated typhoid fever. Tonsillectomy had been performed at the age of 41, because of frequent attacks of sore throat. Constipation had been marked for several years. She had been married fifteen years. The first pregnancy, 12 years ago, had resulted in an abortion at 2 months, followed by such a profuse hemorrhage that the patient had remained in bed during a convalescence of several months. A second pregnancy, 7 years ago, had necessitated delivery by Caesarean section. The child is living and well. The remainder of the past history was unimportant.

The present illness started about four weeks ago, two weeks after a number of teeth had been extracted because of marked pyorrhoea. During the first two weeks of illness, there was no special discomfort except lassitude and weakness. These symptoms were followed by sore throat, non-productive hacking cough, and loss of appetite. The patient continued with her household duties until 9 days ago, when she discovered that she had fever, and went to bed; since then she has had indefinite pains through the chest and abdomen, rather profuse night sweats, and nausea and vomiting after taking solid food. About 17 pounds in weight has been lost during the past month.

PHYSICAL EXAMINATION: The patient was well developed and well nourished. There was a slight yellowish tint to the skin of the body, but no definite icteric color of the sclera. Lips and mucous membranes had a fair color. The gums at the sites of extractions and elsewhere appeared normal. The throat showed nothing remarkable; the tonsils had been cleanly removed. There was no glandular enlargement. There was slight tenderness on pressure over the fifth and sixth ribs in the left mid-clavicular line. A faint systolic blow was present in the pulmonic area of the heart. The systolic blood pressure was 110; the diastolic, 80. The spleen could not be felt definitely; the area of splenic dulness was not increased to percussion. The liver was not

palpable, and the area of hepatic dulness was not increased. Pelvic examination revealed normal findings. The remainder of the examination was normal.

LABORATORY AND X-RAY EXAMINATIONS: A specimen of urine was normal except for the presence of a few red blood cells and an occasional white blood cell. Hemoglobin was 70 per cent (Dare); red blood cells, 4,070,000; leukocytes, 2,650. Differential leukocyte count:—neutrophilic leukocytes, 58 per cent; eosinophilic leukocytes, 2 per cent; basophilic leukocytes, 1 per cent; lymphocytes, 36 per cent; monocytes, 3 per cent. The following day the white blood cells numbered 3,400. Differential count:—neutrophilic leukocytes, 55 per cent; basophilic leukocytes, 1 per cent; lymphocytes, 40 per cent; monocytes, 4 per cent. The blood Wassermann and Kahn reactions were negative. A blood culture was sterile at the end of 6 days.

A fluoroscopic examination and roentgenogram of the chest revealed only a slight increase in lung markings with radiations extending from the hilus toward the periphery. The peribronchial gland shadows were not increased in size. X-ray examinations of the gastro-intestinal tract showed no abnormality. A roentgenographic examination of the mouth showed no pathology at the sites of previous extractions, or elsewhere.

COURSE OF ILLNESS: During four days in the hospital there was a daily afternoon elevation of temperature to 100-100.4 degrees F. The patient returned home after the preceding period of observation. A tentative diagnosis of low grade bacteremia was made, and treatment was started with intravenous injections of gentian violet for two doses on sucecssive days, and then metaphen, 10 c.c. twice daily, for three days.

On March 23, five days after the first blood count, the leukocytes numbered 3,200. A stained smear showed a number of immature white blood cells. Many of these cells were quite large, with round, oval, or indented nuclei. The cytoplasm took a medium blue stain and contained one or two vacuoles in an occasional cell; no granules were present. The nuclei took a lilac stain, and many contained one or two pale nucleoli. The red blood cells showed slight variation in size, and one nucleated red blood cell was seen. There was an almost complete absence of blood platelets. March 26, the hemoglobin was 48 per cent; red blood cells,

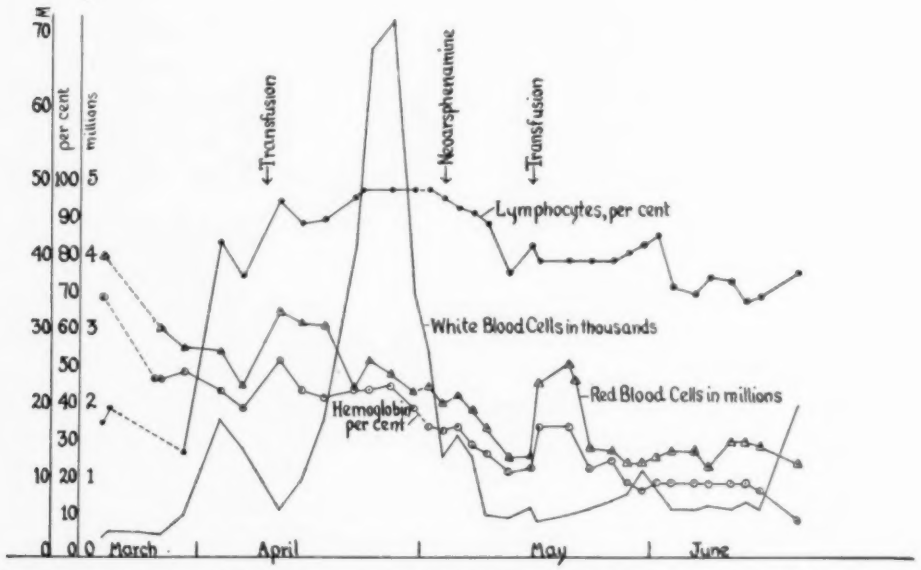

CHART showing the chief features of the blood picture throughout the course of the disease.

3,070,000; leukocytes, 3,000. A stained smear presented the same characteristics as above.

On March 29, the patient was readmitted to the hospital. Her symptoms were unchanged except for increasing weakness. Examination revealed the presence of petechiae at the sites where the tourniquet had been applied to the arms. The yellowish discoloration of the skin had not increased. Posterior cervical glands were palpable on both sides, ranging in size from 5-7 millimeters in diameter. Liver dulness extended from the fifth rib in the mid-clavicular line to 6.5 cm. below the costal margin; the lower border of the liver could be easily felt and was tender. The spleen was palpable about 2.5 cm. below the rib margin and was tender to pressure. Ophthalmoscopic examination showed only retinal pallor.

A specimen of urine was normal except for an occasional red blood cell and a few hyaline and granular casts. The hemoglobin was 50 per cent; red blood cells, 2,830,000; leukocytes, 5,650. Differential count:—neutrophilic leukocytes, 66 per cent; eosinophilic leukocytes, 1 per cent; basophilic leukocytes, 1 per cent; lymphocytes, 29 per cent; monocytes, 3 per cent. A blood culture, clot method, was sterile after 13 days.

April 2, the patient received 10 c.c. of a commercial preparation of leukocyte extract intramuscularly. Two days later, the leukocytes numbered 18,550, with only 4 per cent neutrophilic leukocytes and 85 per cent of chiefly immature lymphocytes. During the past several days, the cervical glands had become larger and firmer, and slightly tender to pressure. There had been blood streaked sputum, and a few petechiae had appeared in the mucous membranes of the mouth. The coagulation time (Boggs coagulometer) was 10 minutes. There was definite icterus. The blood serum gave no direct color reaction with the Van den Bergh reagents, but gave an immediate indirect reaction. The icterus index could not be determined as the clear serum continued to clot after each removal of a previously formed clot. The fasting blood sugar was 103 mgs. per 100 c.c. of blood. A specimen of vomitus contained no free hydrochloric acid.

A diagnosis of leukemia demanded serious consideration, although the influence of the leukocytic extract had to be considered. Blood counts were made at frequent intervals, and the chief features of the blood picture during the course of the illness are shown in the accompanying chart. After April 18, nineteen of the differential leukocyte counts were checked against smears stained to show oxidase granules, at first, according to the technic of Goodpasture,[10] and later, the technic of Sato and Sekija.[11] The percentage of granular cells usually corresponded within 1 to 2 per cent by the Wright and oxidase staining methods. Basket cells or "smudges" were present in all preparations to an extent of 4-5 per cent. Neutrophilic myelocytes were present in most smears, and after May 25, to an extent of about 5 per cent. A few normoblasts and an occasional megaloblast were present in all preparations. Platelets were very rare throughout; attempts to determine the platelet count were unsuccessful, because of their small number, even when using twice the usual quantity of blood. Eosinophilic leukocytes were noted only twice, and this early in the disease; even a moderately severe scarlatiniform dermatitis following the injection of 0.3 gram neoarsphenamine was not accompanied by their appearance. The predominant abnormal cell noted throughout the course of the disease is seen in plate 1, figure 1, while figure 2 shows a higher magnification of the same cell type. (A complete description of these cells appears in the legend of Plate 1). These immature cell forms were considered to

be lymphoid in origin and constituted about 90 per cent of the lymphocytic series. They varied in size from a diameter of about three times that of a red blood cell to a diameter less than that of an erythrocyte; the latter had the apearance of mature lymphocytes. In addition, many unusual and bizarre cell forms were constantly noted in the blood.

Throughout the course of the illness the patient continued to suffer from the same symptoms as in the beginning and increasing weakness. Only the cervical glands became palpable, and these did not exceed 1.0 cm. in diameter. The liver increased in size until its lower border extended 10.5 cm. below the costal margin in the mid-clavicular line; the greatest extent of the spleen was 8.0 cm. below the costal border. Petechiae became rather generally distributed over the body, disappearing almost completely after two transfusions, and then reappearing. Hemorrhages and exudates appeared in the ocular fundi.[12] The gums remained almost free from swelling, and there was only slight bleeding from the gums. For periods of several days at a time there was intense pain with respiration over the lower chest on both sides, accompanied by friction fremitus. Two transfusions were performed with difficulty since all of the superficial veins had been obliterated by intravenous injections. Each transfusion of 700 cc. blood (Unger method) was followed by some improvement in the blood picture, which, however, was overshadowed by the marked aggravation of the patient's symptoms. On both occasions the temperature curve became higher, and sweats, nausea and vomiting increased for a number of days, although there was no immediate reaction from either transfusion. Neoarsphenamine, 0.3 gram, produced no change in the blood picture, but there was a subsequent transient decrease in the size of the liver and spleen. Blood Wasserman and Kahn reactions were again negative, five days after this injection. A third blood culture remained sterile. Two routine agglutination tests for tularemia were reported positive and weakly positive, respectively, but there was no history suggestive of such an infection. A routine agglutination test for undulant fever was negative. Liver extract, 3.0 grams, daily, was taken for 11 days without influencing the blood picture; the reticulocyte count was 0.8 per cent at the end of the administration.

There was a gradual increase in the intensity of the jaundice, with the development of an icteric color of the sclerae. May 2, the icterus index[13] was 27, and eight days later, 24.

Throughout the illness the temperature ranged between slightly subnormal and 102 degrees F., seldom slightly higher. There were some afebrile periods of several days duration. There was a terminal rise to 106 degrees, accompanied by an imperceptible radial pulse. Death apparently occurred from exhaustion.

An autopsy, performed by E.L.B., revealed the following findings: The body is that of an adult female, who looks somewhat older than the specified age. The body has just been embalmed, and there is some rigidity of the extremities. The head and scalp

are negative. The skin presents no abnormality except 15 or 20 dilated superficial capillaries on the upper abdomen and a few small scattered petechiae. There is an old midline scar on the lower abdomen. There are no nodules in the skin. The superficial lymph nodes are not palpable except a few in the cervical regions, and these are rather small and fairly firm. The thyroid is not enlarged. The extremities are negative.

The body is opened by the usual midline incision. There is a very small amount of subcutaneous fatty tissue which is slightly edematous and of light orange yellow color. The chest cavities contain a few cc. of clear fluid; there are no adhesions between the pleural surfaces. The lungs are small and pale, with slight edema and congestion of the bases. There are no areas of consolidation, and no nodules or scarring. The mediastinal lymph nodes are slightly enlarged and rather firm, the largest being about 2 cm. in diameter. None show necrosis; they are solid and semi-translucent. The heart is small and pale, contracted and without gross abnormality; no lesions of the valves or aorta. The intestines are pale, and not distended. The entire gastro-intestinal tract is negative, and there is no lymphoid hyperplasia. The pancreas is negative. The liver is enlarged and paler than normal, with distinct mottling of the surface and within. The gall-bladded is negative. The spleen is enlarged, weighing 850 grams. The capsule is tense and the cut surface is firmer than normal and of greyish red color. No nodules seen. The right kidney is slightly smaller than the left and both show distinct fetal lobulations. The capsules strip rather easily; there is faint mottling of the renal surface. There are no hemorrhages or nodules seen. The renal pelves and ureters are negative. Adrenals grossly negative. The appendix is long and kinked by many adhesions. The uterus has been suspended; no fibroids. The ovaries are small, sclerotic and slightly cystic. The bladder is grossly negative. There is a generalized but moderate enlargement of all the abdominal lymph nodes. None of them exceeds 2 cm. in diameter; they are discrete and show no necrosis on cross section. The cut surface is always semitranslucent throughout.

The microscopic appearance of all organs is essentially the same in a pathological sense. In lymphoid structures there is an obliteration of normal architecture by a diffuse lymphocytic proliferation. In parenchymatous organs there are massive infiltrations or deposits of small rounded non-granular cells. There is little or no actual destruction of tissue anywhere. The lymph nodes show an occasional hyperplastic follicle, but for the most part there is a diffuse growth of small rounded, hyperchromatic, non-granular cells, which in many places have extended out into surrounding fatty tissue. An occasional mitotic figure is seen. There is very little stroma and no necrosis. The spleen shows an occasional follicle which is smaller than normal. For the most part, however, there is a diffuse lymphoid structure, very loose in appearance, with a moderate amount of pigment. Occasional

mitotic figures are seen. The kidneys show a diffuse lymphoid infiltration all through the organs, more marked about the vessels and glomeruli. There is considerable destruction of tubular epithelium but practically no change in the glomeruli. The liver shows the same extensive lymphoid infiltration, particularly about the vessels, but also marked between cords of cells, some of which show atrophy. Some of the liver cells are rather large, and one is seen apparently dividing. There is no cirrhosis; there is slight fatty change. There is a great amount of pigment throughout the liver. The heart muscle shows comparatively little diffuse infiltration, but many capillaries are distended with lymphoid cells. The adrenals show extensive infiltration, as does the medulla of the ovary. The bone marrow shows large numbers of rounded non-granular cells with some small areas of hemorrhage.

Diagnosis: Lymphatic leukemia, with infiltration of all organs.

LEGEND, PLATE 1—WRIGHT'S STAIN

Fig. 1. Five immature cells characteristic of the blood picture. They show a tendency to uniformity in size, but some variation in the shape of the nuclei. One nucleus shows a very distinct nucleolus. A nucleolus is present in two other cells but is much less distinct.

Fig. 2. A higher magnification of three immature cells. The nuclei show coarse chromatin structure with massing of the chromatin about the periphery of the nucleus and the formation of a nuclear membrane. One cell shows two pale nucleoli and each of the others, one nucleolus with massing of chromatin about the nucleolus. The cytoplasm shows a perinuclear pale area. A number of moderate-sized lavender staining granules are present in the peripheral borders of the two upper cells; these granules were noted frequently and were uniformly oxidase negative. The description of these cells, except for the presence of granules, conforms to the conventional description of the lymphoblast. Quite similar cells without granules were sometimes encountered, the nucleus of which seemed to contain 3 to 4 nucleoli.

Fig. 3. The nucleus of the upper cell suggests a stage of amitotic division; the larger lobe contains a definite nucleolus.

Fig. 4. The cytoplasm of the upper cell showed a rather deep basophilic color and a slight ground glass appearance. It contains two distinct purple nuclei.

Fig. 5. A very immature cell with double overlapping mitotic figures. The cytoplasm was deeply basophilic and of a coarse ground glass appearance.

Fig. 6. Probable amitotic division figure.

Fig. 7. Large nucleated red blood cell. The staining of the cytoplasm showed the presence of hemoglobin.

Fig. 8. The larger cell is bizarre in appearance and was rarely seen. The nucleus took a bluish purple stain. The cytoplasm was deeply basophilic except at the tip, where it stained purplish; the cytoplasm had a fine ground glass appearance without granules.

Fig. 9. *This double mitotic figure was seen frequently. It resembles double mitotic figures which were found in the sections from the lymph nodes. It resembles, also, a double mitotic figure from a lymph node illustrated in Cowdry's Special Cytology.[14] The cytoplasm showed a faint basophilia and seemed to be very "thin." The nuclear figures were always purple and had the appearance of having been flattened out.

Fig. 10. *An immature cell with deeply basophilic, nongranular ground glass cytoplasm and distinct double mitotic nuclear figures, similar to Fig. 5. These two cells were the only examples of this type seen. Their appearance suggests illustrations of mitotic division figures occurring in lymph glands pictured in Cowdry's Special Cytology.[15] Erythroblasts?

*Dr. F. M. Johns tells us that he has seen numerous similar mitotic figures in the blood from a proven case of infectious mononucleosis.

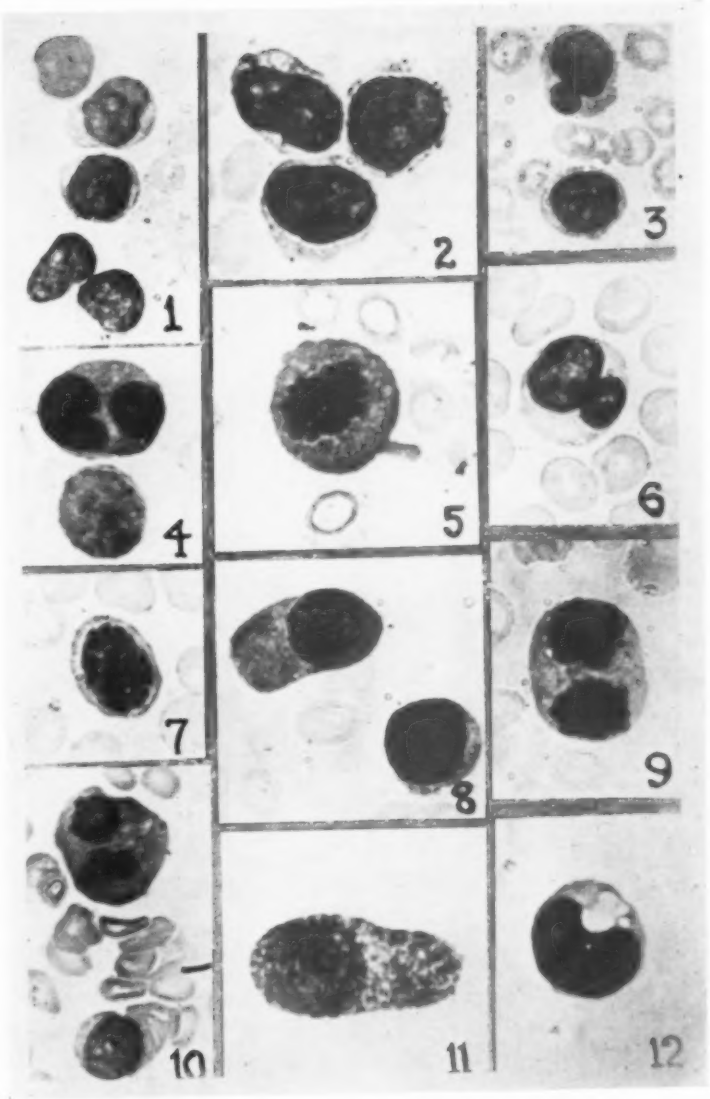

FIG. 1.—Unusual forms of white cells in blood.

Fig. 11. A very large cell with dense purple nucleus, basophilic cytoplasm and a great number of very large purple granules overlying the nucleus and throughout the cytoplasm. The cell is possibly an abnormal myelocyte.

Fig. 12. A phagocyte, containing a portion of an engulfed red blood cell in a vacuole. The nucleus took a deep bluish purple stain, had a dense chromatin structure and contained two nucleoli. The cytoplasm showed a rather marked basophilia. This type of cell was encountered frequently. In some cells a few small rose colored granules were visible in the cytoplasm. Similar clasmatocytes have not infrequently been noted in the blood of patients with acute leukemia;[16] they are usually classified as monocytes.

Discussion

This case presents several interesting and unusual features. During the first several weeks of the disease there was nothing in the clinical picture, the findings on physical examination or the blood picture to suggest the presence of leukemia. The enlargement of liver, spleen and lymph nodes occurred several weeks after the onset of the illness. The leukopenia and the varia-

Fig. 2.—Cellular infiltrations in liver.

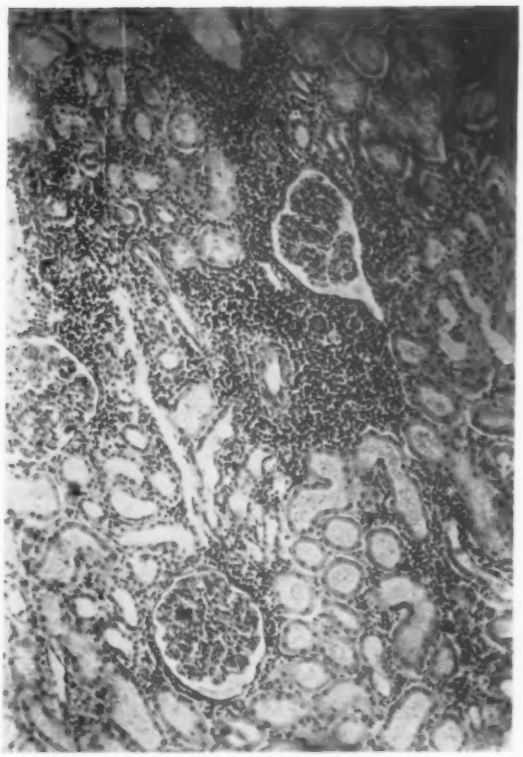

FIG. 3.—Cellular infiltrations in kidney.

tions in the total leukocyte count have been noted not infrequently in other reported cases. With the establishment of a typical clinical picture there appeared a rapidly progressive hemolytic anemia and a rather marked hematogenous jaundice. Such an outspoken jaundice is a rare occurrence in acute leukemia. The frequent occurrence of phagocytic leukocyte forms in the blood arouses speculation as to the rôle played by the clasmatocyte in the destruction of red blood cells in this case. The appearance of many very immature cell forms in the blood is of distinctly unusual interest. Although it was impossible to classify the immature cells, it was interesting that many of them showed a resemblance to cells which are ordinarily found in the germinal centers of lymphoid tissue but not in the blood stream. An unusual clinical feature was the complete absence of ulceration of mucous surfaces and an almost complete absence of swelling of the gums.

SUMMARY

An unusual case of acute leukemia of 4 months duration, probably lymphoid in type, is described. For several weeks there were no findings to suggest the presence of leukemia. The leukemic picture, then established itself rapidly with the appearance of slight glandular enlargement, enlarge-

ment of liver and spleen, petechiae, slight bleeding from mucous surfaces, hemorrhages into the fundi, a rapidly progressive hemolytic anemia and a moderate jaundice. There was a transient high rise in the total leukocyte count but usually the number of leukocytes remained within normal limits or leukopenia was present. The characteristic immature cell agreed in appearance with the conventional description of the lymphoblast. Very unusual and immature cell types were frequently encountered in the blood; double mitotic figures which could not be classified, double mitotic figures resembling cells seen in the germinal centers of lymph glands, rare amitotic nuclear division figures and frequent clasmatocytes containing red blood cells. Blood platelets were greatly diminished throughout. Autopsy findings were moderate glandular enlargement limited to certain chains, splenomegaly and hepatomegaly and lymphoid infiltration of almost all parenchymatous organs.

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Typhus Exanthematicus of the Old World With Reference to Mexican Tabardillo and American Brill's Disease

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TYPHUS fever infection has been known for many centuries. According to Prinzig,[1] during the Napoleon's war period (1812-1814), one-tenth of the German population had Typhus Fever, with a loss of from 200,000 to 300,000 lives. In the Russo-Turkish war, (1828-1829), the loss of both armies was estimated at 115,000, out of which 20,000 died from bullets and wounds, and 95,000 from infectious diseases, Typhus Fever predominating. In Ireland, during the epidemic of 1846-1847, a tremendous loss of lives was encountered.

Eastern Europe, principally Russia and the Balkans, Ireland and Mexico have always been known as countries with endemic Typhus Fever and these sporadic cases not infrequently had blazed up into epidemics. As a rule, the spreading of Typhus Fever coincides with national calamities such as wars, revolutions or any other mass disorders, when the normal conditions of life and accepted hygienic standards are being shattered, destitution, filth, and overcrowding predominate. Hirsh, in his "Historical Pathology" has said, that "the history of Typhus is written in those dark pages of the world's story which tell of grievous visitations of mankind by war, famine, and misery of every kind."

In 1915, the second year of the World War, the conditions in Eastern Europe were such, as to predict that Typhus Fever was going to spread and blaze up into a terrific epidemic with an expected loss of life many times that of bullets and wounds. A short while later, statistics proved that in an astonishing degree. It was estimated that Serbia alone, a small country with a comparatively small army, lost from Typhus Fever, within six months, 135,000 lives. Apparently, Typhus Fever defeated Serbia in a much shorter time than it would have taken the enemy to do so with all the modern inventions used in war. Russia, with a tremendous army, estimated in millions, did not escape the same fate. According to approximate figures given by Martzynovsky,[2] not less than 10% of the whole Russian army were stricken with typhus fever in 1915. And we know very well from the studies of previous epidemics of typhus fever, that once it flares up, it continues persistently at its height for a period of two to three years, then it begins to decline gradually and takes on an as-

pect of an endemic disease with sporadic cases now and then.

Mode of Transmission

Typhus fever is an acute, contagious disease. Direct contact with a patient or with his clothes proved to be a factor in transmitting the disease. Theories and opinions were expressed that the disease could be transmitted through the air. This was based on the supposition that the majority of typhus patients have secondary infections of the upper respiratory tracts, especially bronchitis and tracheo-laryngitis, and by coughing, they contaminate the air with germs. At the present time, as the studies of typhus fever have been greatly advanced, this so called droplet infection theory, has very few followers. There is no doubt any longer that the disease is transmitted by the bite of a body louse, the pediculus vestimenti of hematopinus type, and the blood of the typhus patients is the medium containing the infectious agent. Moczutkowsky,[3] proved that, in 1876, by injecting himself with blood of a typhus patient and producing the disease in himself. Cases have been followed and recorded where physicians developed typhus after accidently cutting their hands during surgical operations on typhus fever patients, infecting themselves with the blood of these patients. That the body lice were the intermediary for the transmission of the disease was experimentally proved on monkeys as early as 1909, by Charles Nicolle[4] at the Pasteur Institution in Tunis. Lice, which had been infected by biting patients suffering from typhus fever were permitted to feed upon healthy monkeys and they subsequently, after a certain incubation period, developed the disease. About the same time, Comte and Conseil,[5] transmitted the virus from infected monkeys to non-infected, by means of bites of lice.

DaRocha-Lima, in his experimental work, was able to infect guinea pigs with typhus fever by innoculation with emulsions prepared from organs of virulent lice, and the most interesting thing was, that those animals on recovery were found to be immune to inoculations with blood from typhus fever patients.

Mexican Tabardillo, quite frequently observed in southwestern United States, though a distinct variety of European typhus, no doubt belongs to the group of exanthematous infections, with practically the same mode of transmission as typhus fever. Moser[6] inoculated guinea pigs with Mexican typhus and found a large number of organisms corresponding exactly to those described by Ricketts and Rocha Lima. That substantiated the theory that the cause of Tabardillo is the same as European typhus. But, there is a difference between these two varieties and the benign type of Brill's disease, which is quite frequently observed and reported in many large Eastern cities, and which also exists in an endemic form outside of seaports and great centers of population.

In Brill's disease, the louse cannot be incriminated. The disease occurs among all classes of people and most careful search has been made in hundreds of cases for body lice, with negative results. Dr. Maxcy,[7] in his extensive study throughout the South-

eastern states, made it clear that the body louse does not play any important part in transmitting so-called Brill's disease. The virus, a mutation of the typhus organism, seems to be carried by mice and never was transmitted from man to man. Fleas and mites probably are responsible for transmitting the parasites of Brill's disease from mice and rats to man, and this is evidently the only source of infection. Brill's own opinion, which is shared by French authors (Netter and others)[8] is, that the disease which bears his name is a variety of typhus fever attenuated by time and by passage through a large number of carriers. The disease, though milder in its course, is almost indistinguishable clinically and serologically from typhus fever of the old world, with the mode of transmission and the causative factor being entirely different.

Clinical Picture

There is a definite incubation period in typhus fever. This period extends from eight to twelve days. Cases have occasionally been seen with a shorter incubation period of four and five days, but those cases could be regarded only as exceptions. No definite clinical manifestations have been observed during the incubation period, though in some cases of the more severe type, three to four days before the onset, patients are complaining of malaise, loss of appetite, general discomfort, indefinite pains and aches. Then comes the fever, with a severe, persistent, agonizing headache, which is not relieved by any antipyretics. Narcotics and cold applications relieve to a certain extent, but only temporarily. Chilly sensations are more constantly observed than chills, and 6 to 10% of patients, do not have any chills or chilliness at all, though standard medical books,[9] referring to typhus fever, stress particularly, that the disease is characterized by abrupt onset with chills. Within three to four days, the temperature reaches its highest point at about 104°-105°, and as the temperature rises, headache increases in intensity. Temperature remains practically constant with slight changes in the form of morning remissions until the fourth or fifth day, when the eruption begins to appear, at first on chest and abdomen and then on the back and extremities. The eruption is not at all characteristic. More than ordinary experience is required to recognize it. Only the hemorrhagic type in the more severe cases, is easily recognisable and could help as a diagnostic point. In the majority of cases, the localization of the eruption will help more than the roseola, which at the beginning looks like the roseola of typhoid fever. But in typhoid fever, the eruption is never seen on the extremities, while in typhus, once it appears on chest, abdomen, and back, it will spread to the extremities with marked predominance on the flexor surfaces. Exceptional cases of typhus have been seen without any eruption, in which cases, an early diagnosis is extremely difficult. When the eruption has not fully developed, dry cupping to the chest will make the exanthem appear before the 5th day. Also, a tourniquet applied for ten or fifteen minutes to the upper extremity, will help to bring out more definitely the roseola, whcih previously

could hardly be seen. These procedures help to differentiate the disease in its early stage from other acute infections (Typhoid or Pneumonia). Within two or three days, the eruption commences to fade away gradually, at first from extremities and then the back, abdomen and chest—just in the reverse order from the way it appeared. In severe cases, the eruption, instead of fading away, turns into hemorrhagic petechiae which remain practically throughout the course of the disease. In those cases, as a rule, the outlook is bad and the course of the disease is more violent. A very interesting point which helps in making an early diagnosis of typhus fever, is the soreness of the gastrocnemius muscles. Patients are extremely sensitive to slight pressure of these muscles and that phenomenon was observed in about 50% of cases as an early symptom. During the period of eruption, the expression of the face is characteristic and rather peculiar. The patient lies on his back with a heavy, listless and dull expression. He is in a stupor. Pupils are small, eyelids red, conjunctiva and sclera injected. Tongue is furred and rather white; teeth are covered with sordes. A very interesting "tongue symptom" in typhus patients was described by Remlinger[10] in 1916. He noticed that typhus patients were always sluggish in showing their tongues. The tongue never protruded beyond the teeth margin and it appeared as though it was restrained by contraction of the genioglossus muscles. That probably explains also the impediment in speech which the majority of patients demonstrate when they tried to talk. It appeared as though they experienced some difficulty in moving their tongues. This "tongue and speech phenomenon" was corroborated by me in a good many cases during the epidemic of typhus fever in south Russia in 1919-1920. Another sign, which is probably due to the same phenomenon and which I also had the opportunity to follow and see in many cases was the difficulty in swallowing. Liquid taken into the mouth was kept there for several minutes by movements resembling those of gargling, and after that was swallowed. It seemed as though time was required to relax the muscles of the pharynx in order to swallow the liquid.

Tracheo-laryngitis is a constant symptom during the first week and this catarrhal condition gradually develops into bronchitis with a moderate cough and expectoration. Indefinite crepitant and fine moist râles are heard in the lower lobes, probably due more to a congestive than inflammatory condition. Breathing is frequent and shallow, pulse soft and rather rapid, though practically corresponding to the temperature. Blood pressure is below normal with systolic pressure falling more rapidly than diastolic, thus lowering the pulse pressure. Ataxic symptoms are present in the form of tremors of the extremities and chin; the latter, when present, being considered a rather grave prognostic sign. Persistent hiccough, one of the manifestations of the subsultus tendinum, and picking at the bedclothes, a sort of athetosis—, are the most characteristic symptoms observed in the majority of cases. Incontinence of urine and feces

is frequent. Nervous manifestations such as headaches, restlessness, and insomnia, which are so pronounced during the first week, gradually subside and prostration appears. Occasionally, restlessness develops into a delirium which is low and muttering in some, wild and hard to control in others. In favorable cases, at about the thirteenth or fourteenth day the temperature begins to drop, and only in about 35%, it drops abruptly by crisis within 24-48 hours. In about 45% of cases, lysis takes places within 3-7 days. Patients begin to sleep soundly, though they still remain for a few days in a sort of stuporous condition. This is the beginning of recovery. In the unfavorable cases, the temperature remains at a high level, coma deepens, the heart shows progressive weakness and pulmonary complications terminate life. Weak heart and prostration favor congestion and edema of the lungs, which were seen in the majority of autopsies. Recovery in typhus fever is a very slow and painful process. The extreme weakness, with a marked hyperesthesia of practically all organs of sensation, is intolerable. Myositis of the lower extremities, particular the gastrocnemius muscles, remains for a long period. Temperature is somewhat elevated for a few weeks, probably due to absorption of toxins. The entire nervous system apparently suffers greatly—irritability, tinnitus and other nervous manifestations present for months. The mortality in typhus fever is in direct proportion to the age; the older the patient, the less chance of recovery. The average mortality for patients 20-30 years of age is 10-15%; 30-40 years of age 15-20%. Women show somewhat lower mortality. The susceptibility of typhus fever and the mortality of this disease in children, is very low. Out of 600 cases of typhus in children, observed in Moscow during the 1919-1920 epidemic, only one death occurred. The severity of the infection is in direct proportion to the duration of exposure to typhus fever, or in the words of Rocha-Lima, "in direct proportion to the numerical content of "Rickettsia", a minute organism isolated by Howard Taylor Ricketts, from digestive tracts of infected lice. The name is used in memory of this scientist, who lost his life in the study of typhus. Rocha-Lima's theory was corroborated by observations made in Southeastern Europe and Russia, during the epidemic of 1915-1919. We were able to prove in good many instances, that those who went to bed during the early manifestations of the disease, had a better prognosis as compared with those who, though not feeling well, continued their daily work, exposing themselves to repeated attacks of lice. This last category of patients had the most virulent infections and those patients were the one's who gave the highest mortality. That particularly could be said about the medical personnel—physicians and nurses, who kept on working under most strenuous conditions all througth the incubation period, exposing themselves over and over again to the bites of lice, working until they actually dropped, and no wonder that the mortality was extremely high, many points higher than the average mortality of the gen-

eral population comparatively. Predisposing factors to typhus fever are numerous, and as in any other epidemic, play a very important part. They are: physical and mental exhaustion, lack of sleep and food, excess in alcohol. Typhus fever is one of the few infectious diseases which confer a strong and permanent immunity after one attack of this disease. It is most unusual to have typhus fever second time. Exceptional cases have been reported in the medical literature, but there is always a doubt of the correctness of the diagnosis.

Bacteriology.

As far back as 1892, Levashov[11] succeeded in isolating from the blood and spleen of typhus patients a motile, polymorphous micro-organism, which he called coccospirillus exanthematicus or spirochaete exanthematici and which he thought was the cause of the disease. Soon after, Levashov's findings were corroborated by many other research workers. Then in 1912, Hlava[12] isolated a rod-like organism, resembling a streptococcus and a diplococcus, which he called streptococcus typhus exanthematici. Ricketts, Prowazek and others[13] were able to isolate a minute organism from the digestive tracts of infected lice, which they stained by the Giemsa method. And in 1915 Da Rocha-Lima proved that those organisms isolated from the gastrium in typhus infected lice, could not be found in lice obtained in typhus free regions.

Plotz[14] in 1914 isolated from the blood of typhus fever patients and those having Brill's disease, a gram-positive bacillus, non motile and non acid-fast, which he thought was the organism causing those diseases. But further experiments and also studies of Schultze[15] (American Red Cross Commission to Poland) showed that the organism isolated by Plotz was only present in typhus fever patients and that it was not the etiological factor of the disease; Plotz had not succeeded in producing the disease—picture in animals, nor the immunity reactions by inoculating animals.

In 1915, two Austrian physicians, Weil and Felix[16] studying the outbreak of typhus fever in Galicia, isolated from the urine of the typhus patients, a gram-negative organism which agglutinated in the patient's own serum, and in the serum from other patients. As the bacterium isolated was of a proteus nature (one of the strains of proteus vulgaris) and only one particular strain-X19 proved to have strong agglutination properties, they called it Proteus X19 and the agglutination test the Weil-Felix reaction. Proteus X19 could never be agglutinated by serum from non-typhus patients and this specificity to typhus patient's serum helped to arrive at a diagnosis in doubtful cases. The Weil-Felix reaction is somewhat similar to the Widal reaction in typhoid and is really a test of the agglutination power of the patient's blood serum, obtained from cases of typhus fever. The reaction is reasonably constant and some workers secured positive results in as high as 97% of cases; Fairley in his work in Egypt showed that 98% of typhus cases gave positive agglutination reactions with the organism while in 120 control non-typhus cases, no

positive agglutinations were obtained. The agglutination reaction appears during the first week of the illness, also at its height and occasionally during convalescence. There is a relation between the age of the patients and severity of the illness on one hand, and the titre of serum agglutinating the organism—on the other. With the older and more severely ill patients, a much higher dilution occurs, while in the younger patients, or in the less acutely ill, the agglutination titre is much lower.

Brill's disease apparently responds also specifically to the Weil-Felix reaction as was shown by Havens[18]. His study in more than one hundred cases of Brill's disease indicated that the reaction was positive in about 95% of cases during the second week, becoming increasingly stronger until convalescence. He proved the specificity of this reaction in Brill's disease by including as controls more than 1000 negative results in other disease conditions. The question whether the organism isolated by Weil-Felix is just a secondary invader and the agglutination properties due to its presence, or the Proteus X19 is the primary cause —is not definitely established. The same thing could be said about "Rickettsia" in reference to the causative agent of typhus fever, as no one had ever succeeded in growing the "Rickettsia" in artificial media. There is also a considerable question concerning the significance of the minute intracellular diplobacillus demonstrated by Mooser[17] as the causative factor of Mexican typhus. So far it has not been definitely proved and agreed that the diplobacillus could produce a typical disease picture in animals.

Few years ago Kusama[19] described a new bacillus which he isolated from the kidneys of Japanese monkeys previously infected with typhus fever. He claimed that he had produced clinically and pathologically similar changes in the monkeys as those produced by the passage virus of typhus. Injection of a large quantity of these organisms which had been made avirulent or killed with phenol developed immunity in monkeys against the passage virus. So. Kusama reasonably believed that he was dealing with an organism causing typhus fever. And yet, in spite of so many bacteriological discoveries, or probably because of so many conflicting findings, the etiology of typhus fever still remains an open question. However, the Weil-Felix reaction being a rather constant feature in typhus fever, apparently enjoys recognition and is being used extensively for diagnostic purposes, during epidemics of that disease.

Pathology.

There are no characteristic macroscopic changes which could be specifically referred to during the autopsy. Typhus fever being a disease of great toxic virulence, the anatomical changes are those of severe fevers. The muscles of the entire body are of a dull-red color and often show granular degeneration and hemorragic infiltration. A general hyperemia of all the small vessels with thrombosis and necrotic changes, is usually present. The heart, apparently suffers greatly during the disease. The muscles of the heart are flabby and fatty degeneration occurs

quite frequently. The pericardium contains moderate amount of fluid. Hypostatic congestion of lungs is very often seen. Liver is quite frequently enlarged and shows parenchymatous degenerative changes (cloudy swelling). Similar changes are observed in kidneys. The spleen is usually of normal size and in the majority of cases without apparent pathological or histological changes. General hyperemia of the lymphfollicles and also marked hyperemia of the laryn, trachea, bronchi and pleura is present in practically all cases. There is a rather frequent occurrence of focal vascular lesions in the brain and less demonstrable in the spinal cord, with a definite increase in spinal fluid protein.

Complications.

The complications depend greatly upon the individuality of the patient, his constitution and resistance. The intellectual patients whose "neuro-complex" is more highly developed, show psychic reactions mostly in the form of a confusional psychosis, while in the majority of all cases, respiratory complications are prevalent. Bronchitis occupies the first place in order of frequency with 75% of all cases; broncho-pneumonia, a more grave complication is next in frequency with about 30-35%. Pneumonia occurs in about 12-15% and almost always at the middle or the end of the second week of the disease when the crisis is expected. It is more of a hypostatic than inflammatory nature and the picture is somewhat different from lobar or catarrhal pneumonia; no rusty or bloody sputum is seen. The sputum is scant and the patient is too weak to expectorate it. In favorable cases these pneumonias resolve within a short period after the temperature comes down to lower levels.

Otitis media and parotitis frequently occur in those cases where the proper hygiene of the mouth, tongue and teeth has been neglected during the course of the disease. Thrombophlebitis as the result of the pathological changes in the endothelium of the vessels—is not infrequently seen. Acute hemorrhagic nephritis, a very troublesome and serious complication, fortunately was seen only in about 5% of all cases.

Summary.

Wars, revolutions and other national disorders are directly responsible for the epidemics of typhus fever, as these conditions destroy the accepted hygienic standards of a normal life.

Typhus fever is transmitted by the bites of the body lice, the pediculus vestimenti of hematopinus type and the blood of the typhus patients is the medium containing the infectious agent.

Brill's disease is never transmitted from man to man; the body louse could not be proved to be the transmitting factor. This disease is endemic in America, milder clinically than typhus fever and rarely causes any fatalities.

Endemic typhus of a stronger virulence than Brill's disease has occurred sporadically in the southwestern states and is clinically identical with Mexican Tabardillo.

Typhus fever is a general toxemia which affects violently the nervous

and the muscular systems; the involvement of the vascular system is exhibited in the small vessels and capillaries.

The recovery in typhus fever is a very slow and painful process; mortality in adults ranges from 10-20%. After middle age, mortality is high. In children the mortality is very low.

Predisposing factors to typhus fever are: physical and mental exhaustion, lack of sleep and food, excess in alcohol, respiratory infections.

The etiology of typhus fever still remains open to discussion; many bacteriological discoveries were reported and practically all of them after years of study were considered as secondary invaders and not as primary organisms causing the disease.

Weil-Felix agglutination reaction apparently enjoys general recognition as a rather constant and specific feature in typhus fever.

The pathological changes of typhus fever are usually those of severe fevers. The muscles, vascular system and the brain suffer apparently the most.

Complications depend greatly upon the habits and the constitution of the patients, though in the majority of cases, respiratory involvement is prevalent. Purpura and subcutaneous hemorrhages belong to the signs of grave prognosis.

One attack of typhus fever in man confers a definite and permanent immunity.

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Tuberculosis: The Nature of the Diagnostic Problem

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IT is now dawning on the rank and file of the medical profession that the diagnosis of pulmonary tuberculosis does not depend on the finding of the tubercle bacillus in the sputum. The days are over when one suspected tuberculosis, searched a few slides for bacilli, and finding none, decided to remove the patient's appendix. The realization is no longer rare that there are many cases, even for advanced ones, without bacilli in the sputum, and even without sputum.

It was comforting to have such a convenient diagnostic test as that to make our diagnosis for us and relieve us of the burden of doing our own thinking; and now that it has been snatched away from us, the mind bent on a diagnosis seems to miss something. The literature is full of attempts at clear-cut methods for making a diagnosis of tuberculosis by some rigid laboratory procedure or some definite clinical sign. The von Pirquet test, the complement-fixation test, the various flank attacks on hemocytology, and no end of physical signs, have covered the pages of journals with enthusiastic words. Not one of them seems to have earned a very solid position. In fact, as scientific observation has made our knowledge of tuberculosis more extensive and accurate, we find more and more solid ground taken away from our diagnostic feet. The realization has been forced upon us that severe pulmonary tuberculosis may be going on in a patient who has no temperature, or in one who has no demonstrable physical findings in the chest. There is not a sign or test that is invariably present or pathognomonic.

We are groping for a sign that will make the diagnosis of tuberculosis a simple, straightforward matter. It has always been human nature to want a "sign". We want some method of diagnosing tuberculosis, that if the test is positive it means that the patient has tuberculosis; if negative, that he does not have it; such that we can turn the patient over to our technician to "work out" while we read the sport page. This may be possible in some disease conditions; the diagnosis of manifest cases of malaria or diabetes or pernicious anemia may possibly be made that way. But the diagnosis of tuberculosis cannot be made that way. And as far as the present state of our knowledge permits of generalization, the nature of the problem is such that the diagnosis can never be made that way.

Why not?

Pulmonary tuberculosis occurs in so many pathological forms and has so many clinical manifestations that we seem to be in the situation of dealing with a considerable number of widely differing diseases, and not with a single entity. Though a result of the same disease, how can manifestations differ more widely than those presented by the patient with cough and sputum, the patient with only gastrointestinal pains, the "nervous" patient with rapid heart and anxiety syndrome, the patient with brachial plexus neuritis, the thin, afebrile patient with reflex throat pains or headache, or the well-nourished, febrile one, with no effort capacity? The caseated or calcified lymph nodes, the fiibrosis at the root of the lung, the discrete scattering of minute tubercles throughout lung tissue, the slight edema and congestion of an upper lobe, the consolidation of an exudative lesion, the necrotic cavity—these differing types of pathology hardly offer any hope of being recognized in the living patient by some open-and-shut, all inclusive technical procedure. They seem to have little in common save the bacillus that produces them.

Yet this one connecting factor, the only thing from a clinical standpoint that puts a common denominator under these many and varied manifestations—the tubercle bacillus—offers no hope of serving as a key to the solution of the diagnostic difficulty. Some test to determine absolutely the presence or the absence of the tubercle bacillus in the body might seem desirable. But, it would be of no diagnostic value to us clinically. For, though the tubercle bacillus is present in the body in all cases of clinical illness, yet it is likewise present in the countless cases that are not ill at all. In civilized communities, practically every adult human being harbors the tubercle bacillus, but only a relatively small number of them suffer illness from it. A test that would absolutely indicate the presence of tubercle bacilli, would be positive on almost everybody, sick or well.

Therefore, an effort to determine whether or not a tuberculous process is present does not constitute a diagnosis. Such a process probably is present; but that is insufficient grounds for assuming that it is necessarily at the basis of the patient's symptoms. There are individuals in whom pulmonary pathology of considerable severity is plainly discernible, and yet who to all practical purposes are well, competent, symptomless, working hard and enjoying life. Conversely, we find persons who suffer from severe symptoms and excessive incapacitation from the slightest of tuberculous lesions.

The diagnostic problem is to determine to what extent the patient's complaint or illness is due to his tuberculous process and to find all possible etiological factors and associated conditions, with a view to formulating such therapeutic measures as are necessary to clinical improvement.

There are many clinical pictures in which tuberculosis occupies most of the view, but in which it is in reality a secondary consideration. A pair of seseverely infected tonsils, the undernutrition consequent upon the treatment of a severe nephritis, the strain of a pregnancy or a lactation, the debility of a hyperthyroid state, all may

result in the flare-up of a tuberculous focus, which originally was no worse than what we all possess within us. But, some pathological condition as just mentioned has caused it to become severe enough to occupy the entire diagnostic foreground, especially if the case is seen thus for the first time. Environmental factors involving stress are especially prominent in fanning these flare-ups. The diagnostic problems in these cases are not merely those of the tuberculosis; they are the problems of a human being under the domination of an environment and with all sorts of pathology.

Cases primarily and purely tuberculous, not involving the influence of these other factors, those caused by heavy doses of early infection or excessive allergy or low immunity, or the localization of metastatic re-infection in vital areas, are relatively in the minority in the general population. These are, however the only cases in which it is justifiable to diagnose and treat the patient as "a case of tuberculosis". All others are problems of a human being who is, either intrinsically or extrinsically maladapted to his environment.

There is no short-cut to the diagnosis, and there probably never will be. The diagnosis can be made only on the basis of, on the one hand a thorough familiarity on the part of the diagnostician with all the phases of the disease, so that the utmost significance of every item in the history, complaint, and examination findings is promptly clear to him; on the other hand of a most complete and painstaking investigation of the patient's body, personality, and past life. The verdict is frequently quite as difficult to arrive at, as is that of a jury concerning the guilt of a prisoner from circumstantial evidence.

A brief review of some of the items of knowledge necessary for the adequate recognition of tuberculosis may be given here, on the basis of the modern views of the various subjects.

Etiology. 1. Tuberculosis is the penalty paid by human beings for civilization. The tubercle bacillus more or less happens to be on the scene, and steps in when opportunity offers. The real cause of tuberculosis is failure of adequate adaptation to environment, the underlying causes of which may lie either in the individual or in the environment. Our latter-day compassion and modern science preserve the life of the unfit individual and then throw him out, unprovided for, into a social system whose intense stresses are telling heavily even upon the most fit. Tuberculosis results when the balance between the individual's capacity and the stress to which he is subjected, is upset. The bacillus is distributed with sufficient profuseness in our civilized environment, to be present and ready to participate whenever the opportunity is favorable. With probably few exceptions, everyone comes into contact with the bacillus and acquires it into his body during childhood, and carries it about with him, ready to get down to business whenever the proper conditions are provided.

The relation of the tubercle bacillus to clinical tuberculosis is about the same as that of the Bolshevik communists to present-day conditions in Rus-

sia. The Bolsheviks did not cause the downfall of the imperial Russian government. This government fell because of its own intrinsic pathology; but the Bolsheviks were organized and at hand, ready to take hold when an opening appeared for them to step into.

2. In addition to the above general principle, various purely accidental factors are responsible for clinical cases of tuberculosis. Infection with large doses of bacilli will cause anything from a swift and quiet death to a severe and prolonged illness. The localization in a joint, a kidney, the meninges, etc., of a lesion which in the lung would remain silent and harmless, produces severe types of the illness. If a caseous focus ruptures into a bronchus, beneficial surgical drainage results, even though the man at the microscope is very much excited; if it ruptures into a vein or a large lymphatic trunk, the miliary and fulminating types are produced. The involvement of a nerve-trunk in an inflammatory area produces a tremendously impressive array of clinical symptoms. The purely fortuitous factor of where the lesion happens to localize, where the bacillus happens to stop and set up housekeeping, determines between silent infection and severe illness. If the lesion is in one place, the patient never knows it; if it is a centimeter away he may die or lead a miserable existence for many years.

Allergy and Immunity. These two terms are not necessarily synonymous, though the two physical states frequently run parallel. They can best be explained by citing examples. Suppose we inoculate with tubercle bacilli an animal that has never before been in contact with them. If the dose is a large one, rapid death without illness or symptoms will ensue. If the dose is small, no apparent effect will be noted. But, there has been an effect, for if the same animal now receives a second small dose, it becomes acutely ill, with temperature, tachycardia, anorexia, loss of weight, and with local inflammation at the site of injection which may extend to tissue necrosis. The animal is now sensitized to the protein of the tubercle bacillus; it is *allergic*. Furthermore, this animal can now be given a dose of bacilli large enough to have killed it promptly the first time, and it will tolerate this dose and recover. It is now relatively *immune* to the tubercle bacillus.

It is allergy that is responsible for the clinical symptoms: on the one hand the "toxemia" syndrome of temperature, tachycardia, anorexia, malaise, loss of weight, etc., and on the other hand the local inflammation and tissue destruction. They are due to the sensitization of the body to the protein of which the tubercle bacillus is composed, and are maintained by the constant absorption of this protein from the existing foci. They are intensified each time there is a new inoculation of the patient with a new supply of bacilli from without or by reinoculation from within. The severity of the allergic symptoms varies (1) directly with the amount of tuberculoprotein being absorbed, and (2) directly with the degree of the patient's sensitization to the protein.

Immunity in tuberculosis is a subject about which little is known. It is some property of the tissues by virtue of which the tubercle bacillus is unable to survive there. An immune animal will survive a quantity of inoculated bacilli that will kill a non-immune animal; but in regard to the mechanism of that immunity we are still in the dark. At the present time there is no proof that allergy and immunity are in any way related, and there is considerable evidence to indicate that they are distinct and independent phenomena.

The Visceral Reflex. By this term is meant the sensory or affector response from a central neurone to afferent stimuli coming from an inflamed or irritated viscus. The path of the stimuli forms a reflex arc with hyperirritated central neurones in the middle. In the case of the lung, the afferent stimuli travel through the vagi and sympathetics to the upper cervical segments. In the presence of an inflammation, these afferent impulses become abnormal, distressing, irritating (though not registered in the upper centers as pain or conscious sensation). The central neurone segment receiving these impulses becomes hyperirritable, and therefore its efferent impulses are abnormal. The abnormality takes on the form of an intensification of the usual efferent effects; muscle becomes hypertonic, glands secrete excessively, skin areas become hyperesthetic. Fatigue and degeneration through long persistence of this state results in eventual atrophy of muscles and relative anesthesia of skin areas.

These effector phenomena of visceral reflexes produce visible and palpable changes in the patient's exterior, and can be used as diagnostic evidence. A knowledge of the neurological principles involved enables the examiner to interpret a great many things concerning visceral conditions from external appearances.

Effector phenomena due to reflexes from an inflamed viscus also appear in other viscera. In lung disease, the increase or decrease of gastro-intestinal tone with accompanying symptoms in the field of consciousness, the effects on the heart rate, on the action of the muscles of the larynx or the eye, operating through the vagi, are quite familiar. To the initiated, abdominal, cardiac, or laryngeal symptoms are frequently a clue to the existence of pulmonary pathology.

Pathogenesis. The great majority of civilized human beings acquire their tubercle bacilli in small enough doses and far enough apart, so that most of them do not become ill and manifest no symptoms worthy of note. If their first dose was anything but minute they would not survive, especially as it usually comes in early childhood. Bacilli acquired subsequently to the first dose become encapsulated, and are held enclosed in a firm wall of fibrous tissue.

As long as this wall holds the host is safe from illness. The factors which hold this wall intact, or weaken it and permit the egress of bacilli depend in the ultimate analysis on the patient's nutrition and on the stresses to which he is subjected, which include mental and physical effort, infection, and ex-

posure. In most peoples' lives there occur some episodes which lower this degree or quality of resistance of the fibrous wall and render it more permeable to the enclosed bacilli. Egress of bacilli occurs, with implantations into areas of healthy tissue, usually in minute quantity. Allergic symptoms follow, as does likewise increased immunity. The new foci plus the old ones, double the number of sources from which reinoculation may take place. Thus, each successive reinoculation is of increased volume; there is an accumulation of the quantity of infection in the patient's body.

In the great mass of individuals, though the process continues to progress through years, the total amount and effect of it is not sufficient to rise above the surface of their good health and well-being. In the person who is ill with tuberculosis, the process differs in degree only, not in kind. Fibrosis is less thorough and firm; reinoculations are more frequent; therefore spread is more rapid and distribution more extensive. The entire process hinges on the less effective encapsulation of the bacilli, due to environmental influences or factors of individual resistance. The patient becomes highly sensitized and allergic effects are severe, with their consequent clinical symptoms and pathological lesions. This all carries with it the increased mathematical probability of a lesion encroaching upon a vital area, a nerve-trunk, a large blood or lymph vessel, a joint membrane, the meninges, a kidney.

With a fundamental knowledge of the above phases of tuberculosis, it is possible to direct one's diagnostic efforts so that in spite of the difficulties and complexities, definite conclusions can be arrived at in regard to the individual patient's status. But, the diagnostic efforts must consist of a complete study of the patient's body and personality and history and environment; no single clinical method or laboratory test can possibly tell the story.

A careful history is of at least as much diagnostic importance as any other one item in the examination. Personally, the writer fails to see how it is possible to entrust the obtaining of the history to an inexperienced interne or junior assistant. Even the experienced mind is busy every moment during the extracting of such a history, and the greatest skill is necessary to elicit essential information. With a properly taken history, however, the diagnosis can frequently be made quite accurately (though tentatively) before the examination proper begins. The story of ups and downs in the physical condition with gradually but steadily decreasing capacity, the obvious influence of environmental factors on the physical state, the clear evidence of reflex effects from the viscera—these things in a history are quite as pathognomonic as the bacilli under the microscope, and of considerably more diagnostic value.

This paper is no place for the discussion of the physical examination in detail. It can only take time to emphasize that the examination must be systematic: which means that there must be a clear and definite purpose in its procedure, with a concrete list of

details to be covered, each subserving the original purpose, and all mapped out beforehand. The examiner must begin at one end and proceed without omission throughout the entire list, allowing nothing to cause skipping or sidetracking of the attention. The chest contains numerous items besides râles and changes in the percussion note; the possible list of chest data numbers over fifty. But, these things are all in the text-books. The examination of the body must be rigidly thorough and complete, and dare not stop with the lungs, because (1) the finding of a clear pulmonary lesion is in itself insufficient proof that the patient's illness or symptoms are due to that; they may be due to some other pathology somewhere else; and (2) even in the plain case of manifest tuberculosis, associated physical defects are frequently the cause of failure to improve. I have seen cases of pulmonary tuberculosis received marked benefit from a herniotomy.

The laboratory is assuming a constantly greater importance in this sphere. It cannot be said to offer much of pathognomonic value; but its work is of immense importance in accomplishing a thorough survey of the patient, in following progress, and in formulating a prognosis. Such things as the erythrocyte count, the Schilling leucocyte count, the blood-sedimentation test, the blood-calcium, a careful urinalysis, a basal metabolic rate determination, should be part of the study of every patient.

The X-ray was for a while hailed as the absolute criterion, on whose films the diagnosis could be ticked off, yes or no. We now realize that its evidence, while valuable, often essential, is not complete. It shows up acute massive lesions well, and is our best means of checking up on old fibrosis. But, in frequent cases it also fails to give a decisive answer to the question: how much of the patient's illness and disability are due to his tuberculosis process? The X-ray is but one link in our chain of diagnostic evidence.

The diagnosis of tuberculosis is not a technic nor a method. It is a mental process, an exercise of the faculties of observation and judgment. Of all the diagnostic instruments available for the purpose of recognizing tuberculosis, the principal and essential one is the doctor's brain.

Medical Men Who Have Attained Fame in Other Fields of Endeavor:

II, Medical Poets.

By Ernest Weinfield, M.D., *New Orleans, La.*

On grounds of ancient heredity the fine arts and medicine should be closely allied, for Apollo, the god of archery, prophecy, music, poetry, culture, the institutor and guardian of civil and political order and the founder of cities, was the father of Aesculapius, the god of medicine.

MEDICAL POETS

MEDICAL men usually are not much given to a serious cultivation of the Muses. In the case of the average practitioner of our noble art—"Life's endless toil and endeavor" with its concomitant hardships and privations, consume the major part of his sleeping and his waking hours.

Let us consider those who have been outstanding in the various fields.

Ancient Medical Men wrote their works in verse as attest:

Nicander (about 150 B.C.) was a physician poet whose extant poems are "Theriaca" and "Alexipharmaca".

Andromachus was physician to the Emperor Nero and wrote in verse.

Sir Richard Blackmore (1650-1729) a doctor, was pronounced by Dean Swift as "England's Arch-Poet." He wrote a heroic poem in twelve books on "Prince Arthur," "Paraphase on the Book of Job," "Satire on Wit," "Elijah," an epic poem in ten books; "Advice to Poets How to Celebrate the Duke of Marlborough," "The Nature of Man," "Redemption," "A New Version of the Psalms," "Alfred" an epic in twelve books; "A History of the Conspiracies against King William," "Creation, A Philosophical Poem."

Arthur Johnston (1587-1641) was physician to King Charles the First. He was "laureated poet at Paris, and that most deservedly" according to Sir Thomas Urquhart. He wrote an elegy on James I (1635) and dedicated a Latin rendering of the "Song of Solomon" to King Charles which won him the patronage of the English royal family. His Latin translation of the Psalms is held to be unexcelled by any other unless it be Buchanan's, and the fact that his translation is still in use sufficiently attests its value and excellence.

Sir Samuel Garth (1661-1719) studied medicine at Leyden and obtained his M.D. from Cambridge in 1691. He was appointed physician in ordinary to George I and physician general to the army. His satirical poem "The Dispensary" (1699) ridi-

culed those physicians who opposed his plan for establishing a free dispensary for poor people. He wrote "Claremont" (1715) a descriptive poem and contributed to a translation of Ovid's Metamorphosis (1717).

Jean Astruc (1684-1766) took his degree in medicine at Montpellier and later became a professor in the faculty there. He became physician to Augustin III of Poland in 1729, to Louis XV of France in 1730 and a member of the medical faculty in Paris in 1731. His chief medical interest was in dermatology. Astruc acquired great reputation as an anatomist and was the author of "Venereal Diseases" (1736). The work which has immortalized him is, "Conjectures as to the Original Material of Which Moses Seems to have Availed Himself in Composing the Book of Genesis (1753). In this he divided the book of Genesis into two parts, on the ground of the use of Elohim (God) or Yahveh (Jehovah).

Mark Akenside (1721-1770) went to Leyden and three years later became a doctor of medicine. In the same year he produced a didactic poem "The Pleasures of the Imagination," his greatest work. Later he produced a collection of odes. In 1761 he was appointed physician to the queen.

Johann Wolfgang Goethe (1749-1832), the greatest figure in German literature, studied medicine purely with a view to the extension of his knowledge. In 1764 he entered the University of Leipsic, and four years afterwards that of Strasburg, in order to qualify himself for the legal profession. In 1771, after taking his doctor's degree he went to reside at Wetzlar. Goethe wrote a drama "Goetz of Berlichingen" (1773), a novel, "The Sorrows of Werther," which made him world-famous. Other dramas were: "Iphigenia in Tauris," "Faust," "Tasso," "Clavigo," "Stella," and "Egmont." In 1775 he went to Weimar which remained his home for the rest of his life. In 1791 Goethe began to apply himself to optics and he published a work on this subject. In 1795 appeared the first part of his "William Meister" and in 1797 "Hermann and Dorothea," a narrative poem in hexameter verse, the characters of which are taken from humble life. "Wilhelm' Meister's Apprenticeship," a novel which has become well known to English readers through the translation of Carlyle and which contains some of the most beautiful songs ever written. In 1805 the first portion of his great masterpiece "Faust" appeared and raised him to the highest rank of literary fame. In 1809 appeared his "Elective Affinities," a novel in which he advanced certain views on the marital relation which disgusted the moralists. Between 1811 and 1814 appeared his autobiography, one of the finest autobiographies in any language. In 1818 beheld the second part of his "William Meister," the "Wandering Years." The "Estöstlicher Divan" a remarkable collection of Oriental Songs and Poems appeared in 1819, and in 1831 his last work, the second part of "Faust."

John Phillips was a physician who sprang into sudden popularity by the publication of a whimsical and clever medley, "The Silver Shilling," which

was followed by an official commemoration of the victory of Blenheim. His greatest achievement was a poem in two books on "Cider" and he was meditating an epic on "The Last Day" when he died at the early age of 33. A curious fact about his writings is that he sounded the praises of Tobacco in every poem except that on Blenheim.

George Crabbe (1754-1832) abandoned the practice of medicine at an early age for the ministry. He wrote "The Quack" who believes wholly in the potence of "oxymel of squills" and also "The Parish Doctor" who first insults the victim whom he kills." Crabbe, who was the satirist of quacks, laments:

"From the poor man's pay the nostrum takes no trifling part away."

Burke helped him to publish his poem "The Library." In 1783 the "Village" appeared which was followed two years afterwards by the "Newspaper." "The Parish Register" appeared in 1807, the "Borough" in 1810 and was followed in 1812 by "Tales in Verse" and in 1819 by "Tales of the Hall." His poems are all characterized by homely truthfulness, simplicity, and pathos.

Johann Christoph Friedrich von Schiller (1759-1805). After having studied medicine and become surgeon in a regiment, he in his 22nd year wrote the tragedy of "The Robbers" which at once raised him to the foremost rank among the dramatists of his country. He moved to Mannheim and his tragedies "Fiesco" and "Cabal and Love" were produced. In 1887 his drama "Don Carlos" appeared. He wrote "The Ghostseer" which was his singular romance, "Philosophical Letters," and "History of the Revolt of the Netherlands Under Philip II." Goethe secured for him a professorship at Jena, and here he lectured on history and published "Historical Memoirs from the Twelfth Century to the Most Recent Times" and his "History of the Thirty Years' War." It was then also, that through the influence of Goethe, he returned with renewed ardor to poetry and produced his finest lyrical poems and ballads. Among these are "The Diver," "The Cranes of Ibycus," "The Glove," and the "Song of the Bell," the finest of German lyrics. It was after 1798 that he published in succession the dramas of "Wallenstein," "Maria Stuart," "Joan of Arc", the "Bride of Messina" and "William Tell," this last his greatest work. He also adopted Shakespeare's Macbeth for the stage. In German literature Schiller stands second only to Goethe, and his works are perhaps read more than those of Goethe.

Samuel Taylor Coleridge (1772-1834) at the age of ten, became a pupil in Christ's Hospital, London, where he remained for eight years and later went to the University at Cambridge. "The Ancient Mariner" (1798) is Coleridge's poetical masterpiece. His next greatest poem is the unfinished "Christabel." He wrote the fragment of "Kubla Khan" and his magnificent ode "France" and "A Day Dream." He wrote for the Morning Post (1799-1802) at the rate of two or three papers a week. Among these were "The Devil's Thoughts," "Fire, Famine and Slaughter." His play,

"Remorse," was successful. Among his prose writings Coleridge were "Aids to Reflection" (1825) "Lectures on Shakespeare" (1811), "Biographia Literaria," two volumes, (1817), "Lyrical Ballads."

Joseph Rodman Drake (1795-1820) graduated from Columbia College in 1816. "The Culprit Fay" is Drake's longest poem. The "Croaker" was a signature adopted by Halleck and Drake, from an amusing character in Goldsmith's comedy of "The Good-Natured Man" and attached to a series of verses appearing from time to time in the New York Evening Post. Politics, music, the drama, and domestic life alike furnished inspiration for the numbers. Of the forty-eight poems of which the whole series was composed, Drake wrote twenty-one including "The American Flag;" Halleck wrote twenty, while seven were their joint compositions. Drake's health failing, he visited New Orleans in the winter of 1819-1820 in the vain hope that change of air and scene would effect its recovery. He returned to New York in the spring of 1820, fatally smitten with tuberculosis at the age of 26. On his death Halleck wrote those exquisitely touching lines: "On the Death of Joseph Rodman Drake."

David Macbeth Moir (1798-1851) who faithfully performed the arduous duties of a medical practitioner in Edinburgh and whose life was almost wholly devoted to the service of his fellows, was the famous "Delta" of Blackwood's Magazine. His poems of some four hundred of which he contributed "Maga", alone fill two large volumes. In prose he wrote "Sketches of the Poetical Literature of the past Half-Century" (1851) which is a standard work on the poetry of his period. Medical treatises also came from his pen. His "Life of Mansie Wauch, Tailor" (1828) is one of the most agreeable of Scotch sketches. In 1831 he wrote "Outlines of the Ancient History of Medicine."

John Keats (1795-1821) was left an orphan in his fifteenth year, he was taken from school and apprenticed to a surgeon at Edmonton, near London. He made a moderately good surgeon, but finding that his heart was constantly with poetry, he gave up his profession in 1817 and began to study hard, preparatory to a literary career. Keats died at the age of 25. His first volume of poems (1817) contained "On First Looking into Chapman's Homer" and "On the Grasshopper and Cricket." His long poem "Endymion" appeared one year later. His "Eve of St. Agnes" (1819) and "Ode to a Nightingale" (1819) are perhaps his two most popular poems. He also wrote "Ode on a Grecian Urn," "To Autumn," "La Belle Dame sans Merci," "Ode on Melancholy," "Lamia," "Isabella" and an unfinished fragment, "Hyperion."

Thomas Gordon Hope (1809-1895) an English poet of note, practiced medicine in East Anglia, later becoming the physician and friend of Dante Gabriel Rossetti. His works include "Poetic Lucubrations" (1828), "Vates: a Prose Epid" (1839), "New Symbols," verse (1875), "Maiden Ecstasy" verse (1880), "A Divine Pastoral," (1883).

Thomas Dunn English (1819-1902) graduated in medicine at the University of Pennsylvania in 1839. From 1852-57 practiced medicine in West Virginia and later engaging in journalism and practicing law. In 1879 he moved to Newark, New Jersey, where he resumed the practice of medicine. He was a member of the New Jersey Legislature (1863-1864) and represented his district for two terms (1891-1895) in the United States House of Representatives. He wrote novels and poems, among which are: "Zephaniah Doolittle" (1838); "Walter Woolfe" (1842); "Poems" (1855); "Ambrose Fecit" (1869), "American Ballads" (1882); "Boy's Book of Battle Lyrica" (1885); "Selected Poems" (1894). He is popularly known by the song "Ben Bolt."

Hendrick Ibsen, (1828-1906) took the course in medicine at the University of Christiana and left only a few weeks before receiving his degree. Throughout his course of medicine his heart was set upon the drama, and it was the success of some of his early work which came to him just before his graduation in medicine that determined his career as a dramatist rather than as a physician. In 1858 he became artistic director of the Norwegian Theatre at Christiana. His best known dramas are :"The Doll House," "Brand," "Hedda Gabler," "Ghosts," and "Pillars of Society." His plays are noted for discussion of social matters.

Charles Robert Richet (1850-) was educated in Paris, taking his degree in medicine in 1877. In 1887 he succeeded Beckland as Professor of Physiology in the medical faculty of the University of Paris and in 1899 was chosen a member of the Academy of Medicine. He is famous for his research into the phenomenon which he named "Anaphylaxis." He received the Nobel Prize in Medicine in 1913. Richet achieved a considerable literary reputation, not only as a writer on scientific subjects but on international peace and other subjects. He published a volume of verse (1875) under the pseudonym "Charles Epheyre."

Paul Bourget (1852-) is a physician but does not practice. He wrote three volumes of verse, two series of essays and many novels. A number of his books treat of medical subjects but the most typical is "Le Sens de la Mort" (1915). Since then he has written :"Lazarine" (1917), "Nemesis," (1918); "Le Justicier," (1918); "Anomalies" (1919); "L'Ecuyere" (1921); "Laurence Altouri," (1920); "Un Drama dans le Monde" (1921); "Nouvelles Pages de Critique et de Doctrine" (1922); "La Geale" (1923); "Coeur pensif, on sait ou il vas" (1924); "Couplets intimes" (1925).

William Henry Drummond (1854-1907) was unofficially crowned the poet laureat of Canada. He wrote: "The Habitant and Other French-Canadian Poems" (1897); "Phil-o-rum's Canoe and Madeleine Vercheres" (1898), "Johnie Courteau and Other Poems," (1901); "The Voyager and Other Poems" (1905) and "The Great Fight" (1907).

Robert Seymour Bridges (1844-1930) the late poet laureate of Eng-

land, succeeding Alfred Austin, has for twenty years practiced medicine successfully, specializing in pediatrics, only dabbling in verse in his leisure moments. He retired from active practice of his profession in 1882. Among his best poems are "Eros and Psyche" and "Achilles in Scyros." A complete edition of his works was published in 1913.

Charles Alexander Eastman (1858-) a well known Boston physician and an almost full blooded Sioux Indian, has given us several volumes of beautiful poetry, and a quantity of priceless information of the life and customs of his people. His books include "Indian Boyhood" (1902), "Old Indian Days" (1907), "The Soul of the Indian" (1911), "The Indian Today" (1915), "Indian Heroes and Great Chieftains" (1918). He also lectured on Indian life and History.

Frederick Peterson (1859-) graduated from the medical department of the University of Buffalo and later studied abroad. He taught pathology at the University of Buffalo and in 1883 moved to New York where he practiced as a Neurologist. His publications include: "Poems and Swedish Translations" (1883); "In the Shade of Ygdrasil" (1893); "Nervous and Mental Diseases" (1920); American Textbook of Legal Medicine and Toxicology" (1903); "A Song of the Latter Day" (1904) "Chinese Lyrics" (1916); "The Flutter of the Gold-Leaf" (1922).

Francis Thompson (1860-1907), the son of a doctor, studied medicine at Owen's College, Manchester, but took little interest in the profession of a doctor. He was bent on literary productions and published his first volume of "Poems" in 1893. Later he wrote "Sister Songs" (1895); "New Poems" (1897); and in 1905 published a treatise on "Health and Holiness". He is especially remembered for his beautiful poem "The Daisy" and his magnificent one "The Hound of Heaven."

John McCrae (1872-1918) became a fellow in pathology at McGill University and collaborated with Professor Adami on a text book on that subject. He was physician at the Alexandra Hospital when the war broke out, and was among the first to offer his services, going abroad with the Canadian Field Artillery. During his active life as a physician he published poetical compositions, some of which gained considerable popularity. He was killed in service. His touching poem "In Flanders Field" was the most famous piece of verse written during the war.

Jean-Louis Faure, a successful practicing surgeon, has published several books. The most important "L'Ame du Chirurgien" is an ornament to literature.

Lucien Groux, although a surgeon, has bent his effort towards interrogating the Beyond and has published a number of books on immortality.

Georges Comuset studied medicine at the instigation of one of his masters, though he had made brilliant progress in mathematics and drawing. He did not practice medicine long but turned to literature. Some of his verses are considered masterpieces, and he has published many books. Most of his sonnets, devoted to medical sub-

jects, treat lightly and mock-pleasantly the members of his profession.

Leon Daudet (1867-) studied medicine for ten years. In 1894 he took up literature, writing many novels and articles in the "Figaro," "Gaulois," "Soleil," "Le Libre Parole." In 1908 he founded with some friends the royalist journal, l'Action Francaise." He is a member of the Academie Goncourt. His works include: "Hoeves"; "Les Idees en Manche"; "Le Voyage de Shakespeare"; "Suzanne,,; "L'Avant Guerre"; "Hors du Joug Allemand"; "Le Cour et l'absence."

Baron Henri de Rothschild (1872-) is a doctor of medicine and is Medecin-chef de la Polyclinique Hospital de Rothschild. He devotes his leisure to literature and writes under the name "Andre Pascal". Some of his writings other than technical works are: "La Sauve" and "La Rompe".

Pearce Bailey richly deserves to be called a man of letters.

William Carlos Williams of Rutherford, New Jersey, is a practicing physician who has received the "Dial's" award for 1926 for his outstanding contribution to American literature. He is the author of prose and verse. Among his writings are "Marianne Moore"; "The Methods of R. Burke"; poems: "Struggle of Wings"; "Tree"; "March is a Light"; "Young Sycamore"; "Lines on Receiving the Dial's Award"; "Paterson"; "Poets of the Quattrocento"; "M. Moore"; "Bull"; "Full Moon"; "Jungle"; "Lonely Street"; "Poem"; "Sprouts"; "View"; "When Fresh, It Was Sweet"; "Wild Orchard"; "Widows Lament in Springtime".

Physicians also wrote non-medical works in verse:

Thomas Lodge (1558-1625) was an English poet and dramatist and wrote the famous pastoral "Rosalynde Euphyes' Golden Legacie" (1590) which supplied Shakespeare with the plot of "As You Like It". Lodge's dramas were: "The Wounds of Civil War" (1594) and "A Looking Glass for London and England" (1594).

Paul Gottlieb Werlhof (1699-1767), court physician at Hannover, was a great friend of Haller, and, like him wrote poems in the German language and medical works in Latin.

Albrecht von Haller (1708-77) was an infant prodigy, writing Latin verses and a Chaldee grammar at ten. He wrote poems and historic novels. His "Versuch schweizerischer Gedichte" (1732) was the subject of the famous literary quarrel between Bodmer and Gottsched as to the relative merits of the natural and the artificial in poetry. His poem, "Die Alpen" (1729) first drew attention to the glorious beauties of Swiss mountain scenery.

Henry Vaughn (1622-95) wrote "Silex Scintillans or Sacred Poems and Private Ejaculations" (1650) and "Retreat".

James Grainger (1721-66) wrote "Ode to Solitude" and "The Sugar Cane".

Edward Jenner (1749-1823) wrote occasionally in verse examples of which are: "Address to a Robin" and "Signs of Rain".

Robert Southey (1774-1843), although never graduating in medicine was for a time a medical student. In 1813 he was appointed poet laureate.

Among his poetical productions may be mentioned: "Joan of Arc", "Thalaba", "Madoc", "The Curse of Kehama" and a "Vision of Judgment". Among his prose: "Life of Nelson", "Life of Wesley", "History of Brazil" and "The Doctor".

Thomas Trotter (1760-1832) after a rather turbulent career as a surgeon in the Royal Navy retired to Newcastle upon Tyne. In 1829 he published "Sea-weeds, Poems Written on Various Occasions, Chiefly during a Naval Life."

John Mason Good (1764-1827) translated Lucretius into blank verse as he trudged through the streets of London to do his practice.

Jacob Bigelow (1787-1879) published in 1855 an anonymous volume of clever poetical travesties entitled "Eolopoesis."

John Kearsley Mitchell (1798-1858) like his son Silas Weir Mitchell was talented in poetry and fiction as well.

George Friedrich Louis Stromeyer (1804-1876) was a poet and also wrote an attractive autobiography.

Jacob Henle (1809-1885) was a poet as well as an accomplished musician and artist.

Adolf Kussmaul (1822-1902) distributed among his friends, an Christmas day, 1893, a volume of poems, privately printed under the pseudonym "Dr. Oribasius." His "Jugenderinnerungen" (1899) is one of the best of medical autobiographies.

Sir Henry Halford composed elegant Latin verse—"Nugae Metrical"—(1842) as he drove from one noble sick room to another.

Richard von Volkman (1830-1889) was a poet who wrote under the name of Richard Leander. His "Dreams by French Firesides" (1871) is a charming book.

Silas Weir Mitchell (1830-1914) was a poet and writer of fiction and except for some unsigned verses in 1857, published nothing for popular consumption until over fifty years of age.

Henry Havelock Ellis (1859-) published in 1925 his "Sonnets with Folk Songs from the Spanish."

Sir Edmund Gosse (1849-) wrote in verse: "On Viol and Flute" (1873), "King Erik" (1876), "New Poems" (1879), "Firdausi in Exile" (1885), "In Russet and Silver" (1894) "Hypolympia" (1901), "The Autumn Garden" (1908) and "Collected Poems." Among his prose are: "History of Eighteenth Century Literature" (1889), "History of Modern English Literature" (1897) "Father and Son" (1907, crowned by the French Academy 1913), "Aspects and Impressions" (1922) and "More Books on the Table" (1923) and "Silhouettes" (1925).

Sir Donald MacAlister (1854) wrote "Echoes" (1907, 1913 and 1923).

Henry Head (1861-) wrote "Destroyer and Other Verses" (1919).

David Rorie (1867-1919) wrote "Cults," "The Auld Doctor and Other Poems and Songs in Scots" (1920) and has published numerous papers on Folklore and Folk-Medicine in Folklore. His songs include: "The Lum Hat" and "The Pawky Duke" in the British Students Song Book.

Francis Brett Young (1884-) wrote in verse "Fever Trees," "104 Fahrenheit" and "Five Degrees South." He also wrote a play "Captain Swing" (1919) and music "Songs of Robert Bridges."

Charles Mercier wrote "The King's Fishing" (1913) which contains "The Vanity of River Fishes" an ode in imitation of Dr. Samuel Johnson "The Vanity of Human Wishes."

Sir Charles Sherrington wrote "Assaying of Brabantius and Other Verse" (1925).

Sir Ronald Ross (1857-) wrote "Philosophies, Psychologies and other Poems" and a novel: "The Revels of Orsera."

Kenneth Rogers of Bromley wrote "Thoughts of a Nature Lover," "The Tragedy of King James III" and "The Musings of a Medico."

Fred Brush (1871-) the medical director of the Burke Foundation in New York wrote "Susquehanna," "A Dutch Hill Picnic" and "Starucca Dan."

Edwin Nash has just published his "Random Rhymes and Poems for Home Folks."

Louisa Kerschbaumer, the German-American physician has just published a volume of poems, "Denken und Träumen."

James B. Naylor, a graduate of Starling Medical College of Columbus, Ohio, practicing in his home town of Malta, Ohio, and one of late President Harding's most intimate friends, is the author of that much played song, "A Hot Time in the Old Town" and also "Casey Jones."

Edward Willard Watson, of Philadelphia, a graduate of University of Pennsylvania, has produced four volumes of exquisitely written poetry.

Editorials

THE ETIOLOGY OF PSITTACOSIS

In 1879 Ritter observed a house epidemic of severe pneumonia which he thought could be referred to a contagion from parrots, or rather from the cages in which the birds had been confined. The clinical and pathological pictures were those of an atypical pneumonia. Ost saw similar cases in 1882, and Wagner observed the same in 1882 and 1886. In 1891 the affection was introduced into Paris by some parrots imported from South America. In 1892 there was an epidemic of this disease in this city, in which fifty individuals were affected. During the next four years scattered cases were observed in Paris, and advantage was taken of the opportunity for a detailed study of the disease. According to the Parisian observers psittacosis is an infectious disease occurring in parrots and transmissible to man. In parrots the affection is of the nature of a chronic enteritis, characterized by diarrhea, wasting, loss of appetite and falling of feathers. In man the symptoms suggest a grave typhoid, with diarrhea and a malignant atypical pneumonia. After a period of incubation lasting from seven to twelve days, the symptoms begin with malaise, epistaxis, and digestive disturbances, followed by bronchitis and pneumonia. Pulmonary symptoms are always present. There is high fever lasting from three to four days, and falling by crisis. A small amount of albumin is found in the urine. The spleen is usually enlarged. There is a recurrence of the symptoms in the same order, and this may be repeated several times, when finally the fever falls by lysis. The entire process lasts about thirty days. Sometimes there may be a roseolar eruption present. In some cases petechiae may be present. The prognosis is good, if complications do not occur. In the Paris epidemic the mortality was about 37 per cent; in the majority of cases, death was due to pneumonia. The relation of the affection of parrots to the disease in man was definitely proved. The gold-crowned Amazon parrot is apparently wholly responsible for the human cases. Similar cases were seen also in Italy and Germany. Up to 1928, one hundred and sixty-four cases of psittacosis have been reported in the literature, with fifty-four deaths. During the last year the most extensive epidemic of the disease yet reported took place, over five hundred cases being recorded during the autumn and winter months. These cases were well scattered through central Europe, South America, the United States and Hawaii. Although better opportunity was afforded for a more detailed study of the symptoms but little that was new has been added to our knowledge as far as the clinical

picture is concerned. No absolutely pathognomonic symptoms were observed; and the differential diagnosis from influenza, typhoid and pneumonia may be very difficult. The history of contact with a sick parrot is still the chief determining factor of the diagnosis of psittacosis, and until the etiological agent is discovered will probably remain so. According to the views of Nocard the causal agent of psittacosis is a specific bacillus resembling the typhoid bacillus. It is a thick short, motile bacillus with rounded poles, and is a facultative aerobe. It does not stain with Gram's method, does not ferment sugar, nor coagulate milk, nor produce indol. The organism is very virulent; subcutaneous injections in rabbits, mice and pigeons kill within from 14-28 hours. In the Paris epidemic the bacillus was not found in the human body, but three years later, Gilbert and Fournier found it in one case. Palmidessi found an organism in parrots suffering from a diarrheal disease which he regarded as identical with that observed by Nocard. Other observers have failed to find the Nocard organism. Nicolle reported an epidemic of eight cases, four of which were fatal, in which the Nocard bacillus could not be found, but the serum from these cases produced a typical agglutination of a culture of the bacillus furnished by Nocard in dilutions of 1 to 50. At the "Robert Koch Institute" in Berlin during the last winter an investigation of material from animal and human cases of psittacosis has been carried out. The results have recently been reported by Levinthal (Klin. Wchr., April 4, 1930). In no case has the Nocard bacillus or any organism of the paratyphoid group been found. On the other hand careful investigations, the details of which cannot be given here, showed that the etiological agent of South American parrot psittacosis belongs in the group of filtrable viruses, both in the acquired form of the disease and in that transmitted by parenteral injection and by oral inoculation. Infectious material obtained from three different parrots dying of a disease that had produced illness of a severe nature in human beings exposed to them, proved to be virulent after repeated filtrations through Berkefeld-V filters. Comparisons of inoculations of the unfiltered and filtered material show the same incubation period with each indicating that repeated filtration does not diminish the amount of virus passing the filters. Levinthal's investigations confirm those of Bedson, Weston and Simpson in London. While at first the English observers worked with material derived from one parrot only, they succeeded later in obtaining the infection from other infected animals, from experimentally inoculated parrots and through inoculation of the blood of infected human beings. They determined the filtrability of the virus beyond any doubt, using the Chamberland filter L1. The pathological findings in the experimental animals are uniform. There is a soft congested spleen, congestion and venous stasis of all the abdominal organs. At the point of intramuscular injections brownish focal necrosis occurred. The lungs showed in almost all cases a pneu-

monia varying from small localized areas to bilateral complete hepatization. In all cases there was a more or less severe pericarditis; and the myocardium itself showed petechiae or larger hemorrhages. The bacteriological cultivation of material from all organs, pericardial fluid, heart blood and bone-marrow was in all cases negative under aerobic conditions. The anaerobic cultures were not yet completed. Direct microscopic examination of smears showed no ordinary bacteria, as was to be expected from the filtration experiments. On the other hand, the intensive staining of smears made from the clear superficial portions of the pericardial fluid, with Löffler's methylene-blue, or the Manson or Romanowski stains showed either isolated or abundant masses, lying free and in the endothelial cells, of extremely small, sharply contoured, oval bodies, often in diplo-form, rarely in short chains, which showed beautifully in Gram preparations and prolonged fuchsin staining. In all preparations coccoid bodies lying at the border of microscopic visibility were present. Also coccoid and diploforms were found in the Berkefeld-filtrate of the pericardial fluid after it had been diluted fifty times. Levinthal concludes that these extremely small filtrable coccoids are the etiological agent of psittacosis. Confirmation of the filtrability of the virus has recently been given by Krumwiede of New York, and by Pesch of Cologne. In the course of the experimental work on psittacosis at the Hygienic Laboratory in Washington, tissues from fourteen parrots and parrakeets used in the work were examined by Lillie (Public Health Reports, April 11, 1930). The experimental work resulted in a laboratory outbreak of the disease, evidence that the virus of psittacosis was being worked with. In three parrots of this group there were found focal lesions and minute intracellular coccoid and bacilliform inclusions. The lesions were paralleled by some of those seen in material from the first human case of the laboratory outbreak, and precisely similar inclusions were seen in the lungs of that case. In the human case (exposed to six parrots, taken ill January 25 and died February 8) the liver showed focal coagulation necroses, infiltrated with polymorphonuclear leucocytes. The epithelioid cell nodules seen in the parrots were present also in the human case; multinucleate giant cells of rather unusual type were found in these. No inclusions were seen. In the pneumonic lung, where the exudate was composed largely of fat-laden large monouclear cells, a few of the latter were filled with closely packed minute coccoid and bacilliform inclusions staining deeply blue with Giemsa. They were estimated as between 0.2 and 0.3 micron in diameter and possibly 1.0 micron in length. A tendency to denser polar granule formation was noted. In the other parrots and parrakeets in which no focal lesions were found no such inclusion bodies could be demonstrated. Morphologically the inclusions seen in the three parrots and in the human case were closely similar. In all they were Gram-negative, stained well by such methods as Giemsa or phloxin, orange G., and

methylene blue, and often the formation of distinct deep blue polar granules in a light blue rod could be made out. In the parrot and in man they occurred in dense masses within cells of the monocyte, reticulo-endothelial or mesothelial type. Lillie proposes the name *Rickettsia psittaci* for these inclusions and defines the species as "minute Gram-negative intracellular coccoid and bipolar bacciliform bodies of about 0.2 to 0.3 micron diameter, found in reticulo-endothelial cells, mesothelial cells, and large mononuclear cells of the parrot (probably Amazon species), and in large mononuclears in man, associated with, but without established relationship to psittacosis." Whether these bodies are identical with those previously reported by Levinthal and regarded by him as the etiologic agent of this disease, remains to be seen, but the confirmation from various works of the filtrability of the virus makes it practically certain that psittacosis is caused by a filtrable virus. This disposes of Nocard's bacillus as having anything to do with the etiology of the disease. Apparently out of the past winter's epidemic there will come the definite establishment of psittacosis and its etiologic agent, in nosology. It is extremely interesting that the last two decades have seen the establishment of Tularemia and Undulant Fever as distinct nosological entities, and one wonders if there are yet any other new diseases to be separated clinically and etiologically from the great mass of febrile diseases, more or less associated with respiratory symptoms, grouped under influenza, grippe, pneumonia and typhoid-like conditions.

Abstracts

Electrocardiographic Diagnosis of the Artery Occluded in Cardiac Infarction. By W. J. Rose and Frank Meyers (Proc. of the Soc. f. Exper. Biol. and Med., April, 1930, p. 681).

Changes in the electrocardiogram due to cardiac infarction have been noted by many observers, and reports of clinical cases give us our most valuable information because the coronary system in the common laboratory animal does not parallel the human coronary circulation. It is not possible to study the effect of infarction in various parts of the animal body by laboratory methods and apply these findings to human cases. As the result of clinical observations controlled by autopsy findings, these authors conclude: 1, Infarction of the anterior wall of the left ventricle is always associated with occlusion of the left coronary artery. Infarction of the posterior wall of the left ventricle, in the absence of anomalies, is almost always associated with occlusion of the right coronary artery; 2, When the infarction involves the anterior wall, the elevation of the R-T segment of the electrocardiogram is in Leads I and II, and conversely when in the posterior wall, the elevation of the R-T segment is in leads II and III; 3, Knowing the rôle of the right coronary artery in the supply of the posterior wall of the left ventricle, when we encounter a case of coronary occlusion in which the electrocardiogram shows R-T deviation in leads II and III, we can say with reasonable certainty that the occlusion is in the right coronary artery provided there be no anomaly of that artery; 4, It has been demonstrated that the site of infarction and artery occluded can be accurately located during life.

Effect of the Luxus Consumption of Meat Upon the Kidney of the Albino Rat. By R. A. Moore and F. A Hitchcock (Proc. of the Soc. f. Exper. Biol. and Med., April, 1930, p. 706).

Twenty-three albino rats were kept on a high protein diet of 64 calories daily, 36 per cent of which was furnished by protein. The control group of 20 animals was given 55 calories daily, 29 per cent of which was protein. Blood pressure estimations of 8 of the control and 7 of the experimental animals showed no significant variation. Kidney weights were determined on 8 of the control and all of the experimental animals. The average weight of the kidneys of the experimental group was 14 per cent higher than that of the controls. This is 2.2 times greater than the probable error, and the difference is therefore significant. Histological examination was made of both kidneys of all animals. All the animals in the control group showed normal kidneys. Of the experimental animals 17, or 74 per cent, showed some pathological change. These changes consisted of focal areas of fibrosis and cellular infiltration in the cortex, dilatation of the cortical tubules with hyaline casts, and slight to moderate thickening of Bowman's capsule. None of these changes is analogous to human chronic diffuse glomerulonephritis. They conclude, therefore, that in the albino rat a high protein (meat) diet produces no change in systolic blood pressure, but does produce a hypertrophy of the renal substance and certain histological changes which are not, however, analogous to chronic nephritis in man.

On the Treatment of Exophthalmic Goiter with Ergotamin. By Robert Platt (Klin. Wchr., February 8, 1930, page 258).

Since the experimental work of Stoll and Spiro, Löffler, Abderhalden, and Wertheimer

showed the action of ergotamin to be antagonistic to the sympathetic and to the action of thyroxin, many workers have employed this substance in the treatment of exophthalmic goiter, with contradictory results. Platt reports the effects of ergotamin administration to three cases of Basedow's disease. He concludes from his observations that the published experiences with this drug in the treatment of exophthalmic goiter are contradictory, and do not take into consideration the effect of rest in bed and the psychical factors. Platt saw no significant improvement that could be ascribed to the action of ergotamin. In one of the patients so treated there developed unexpectedly a severe vascular spasm of the lower extremities. Although gangrene was avoided with the aid of numerous injections of scopolamin, this case showed that ergotamin may produce dangerous symptoms, without influencing the disease for which it is being used. Even by using ergotamin in over doses no influence on the exophthalmic goiter could be seen.

Urorubin, A New Coloring Matter in the Urine. By M. Weiss (Klin. Wchr., Feb. 8, 1930, p. 148).

Under the name Urorubin, Weiss describes a new coloring matter found in the urine, which arises through the action of daylight upon a chromogen to which the name of urorubinogen has been given. This coloring matter appears to show some relationship to diabetes, to diseases of the heart and bloodvessels, to many infectious diseases, especially to tuberculosis, and convalescence after catarrhal jaundice. Its presence can be determined only on spectroscopic examination. Its chemical nature is unknown; it is most probably a product of the endogenous metabolism. Diet has no influence upon its production. It has not been found in the blood serum, stools or bile. It shows no relation to the coloring matter of urobilin or the tryptophan group. It is also not a lipochrome in the ordinary sense. It gives no blue color with sulphuric acid. Both it and its chromogen can be extracted from the urine by ether, chloroform or benzol. It will be destroyed through evaporation to dryness. It is very sensitive to light, and in the dark will disappear from the urine in a few days. Its alcoholic solution is more permanent the more pure it is. It has not yet been possible to purify it wholly from urobilin. Potassium permanganate will destroy it. Neither it nor its chromogen will give any of the known urine reactions. It cannot be precipitated with acetic or hydrochloric acid. Whether the urorubinogen differs essentially in its chemical reactions from the urorubin has not yet been determined. In old people the presence of urorubin in the urine should be taken as indicating a disturbance of the sugar metabolism. Further clinical work, together with chemical studies will be necessary to determine the nature and significance of this new urinary pigment.

The Effect of Liver Diet Upon the Healthy Individual. By K. Neidert and K. Bannasch (Zeitschr. f. Klin Med., 111, p. 292).

Eight healthy young males were fed 500 g. of liver daily for 12-32 days, and the blood changes were carefully studied. In fifty percent of the cases the hemoglobin content of the blood showed a definite increase, in one person as much as 17 per cent. In all eight cases the red blood cells increased from 400,000 to 1,000,000. In 7 of the 8 cases the granulocytes increased definitely, and reached a maximum of 12-17 per thousand. The white cells remained unchanged. The bilirubin content of the serum increased, but did not exceed the upper limits of normal. In all cases there was a well-defined urobilinuria. These changes speak for an influence upon blood-formation through liver diet, and is opposed to the theory of Jungmann that it inhibits blood destruction.

Lactic Acid Determinations in the Blood of Cases of Myasthenia. By J. Friesz and E. Nohos (Deutsch. Arch. f. Klin. Med., 164, p. 356).

For some time the question as to the part played by lactic acid in the chemistry of persons affected with myasthenia gravis has been attracting attention, and the opinion has been growing that disturbances of lactic acid production may be at the bottom of this disease. Two cases of the disease studied by Freisz and Nohos showed in the rest-

ing state normal quantities of lactic acid in the blood; after moderate exercise there was a marked increase of the lactic acid content of the blood with a corresponding fall in the blood pH. The inorganic phosphorus and blood sugar remained unchanged. It seems probable that this disease is dependent upon a disturbance in the resynthesis of the lactic acid.

Toxic and Septic Processes in Scarlet Fever as the Basis for a Judgment of the Therapeutic Possibilities of Antitoxic Serum. By v. BORMANN (Z. f. Kinderheilk. 48, p. 313).

Observations in a large scarlet fever epidemic led v. Bormann to a new conception of the etiology of scarlet fever. The initial stage consists of two components: a toxic and septic. In the first stage there is developed the toxic effect of the streptococci, which prepares the way for the direct invasion of the streptoccocci through the lymphatics. This second septic stage is the basis of all the complications of scarlet fever. This observation is further confirmation of the work and views of the Dicks.

Therapy of Coronary Thrombosis. By R. SINGER (Wien. Arch. f. inn. Med., 18, p. 421).

Singer advises that the term coronary obstruction be used in place of coronary thrombosis, inasmuch as endarteritis of the coronaries and embolism may produce the same clinical picture as that of thrombosis. Nitrites do not influence the continuous severe anginal pain of coronary obstruction. Increase of temperature is often present. Out of 20 cases observed by him 5 died in the first attack, 2 in the next 8 weeks. Absolute rest in bed is indicated, with the use of morphine, in spite of the theoretic consideration that as a vagotonic drug it narrows the coronary arteries, quinidin, and later euphyllin. Digitalis should be given only if symptoms of decompensation are present. The Zülzer cardiac hormone, as well as röntgen irradiation may be tried.

Reviews

Human Biology and Racial Welfare. Edited by EDMUND V. COWDRY, Professor of Cytology, Washington University, St. Louis. With an Introduction by Edwin R. Embree. 612 pages, 11 figures. Paul B. Hoeber, Inc., New York, 1930. Price in cloth, $6.00 net.

This book is written for two groups of readers. First, for students who are about to specialize and can do so more intelligently after they have seen in perspective what lies ahead. This applies particularly to medical students who in order to be good physicians must above all be good biologists. A knowledge of what is known of human life, past, present and possible future, is for them essential. In the second place, it is hoped that the book will be of interest to readers of mature years occupied both in science and in business who have an inquiring turn of mind and wish to look a little below the surface. In this way it may assist in the movement in favor of adult education which is gaining momentum in the United States and is destined to spread. The book is divided into five parts: Part I, *Perspective*: Life in Space and Time, by Henry Russell. Part II, *The Origin of Man*: Evolution Traced Biochemically, by A. B. Macallum; The Animal Ancestry of Man, by William K. Gregory; The Evolution of the Brain, by George H. Parker; Mental Evolution in the Primates, by Robert M. Yerkes; Societal Evolution, by W. M. Wheeler; and Human Races, by A. Hrdlicka. Part III, *Man as a Physiological Unit* consists of the following chapters: The Vital Units Called Cells, by E. V. Cowdry; The Relation of Cells to One Another, by Alexis Carrell; The Integrative Action of the Vascular System, by W. B. Cannon; Nervous Integrations in Man, by J. F. Fulton and C. S. Sherrington; and The Integration of the Sexes—Marriage, by Clark Wissler. Part IV, *Effects of Environment* contains the following chapters: The Effect of Climate and Weather, by Ellsworth Huntington; The Reaction to Food, by E. V. McCollum; The Influence of Urban and Rural Environment, by Haven Emerson, and Earl B. Phelps; Antisocial Behavior: Delinquency and Crime, by William Healy; Adjustment to Infectious Disease, by Hans Zinsser; What Medicine Has Done and is Doing for the Race; by Sir Humphrey Rolleston; The Relation of Science to Industry, by R. A. Millikan; and The Influence of Education, by John Dewey. Part V, *The Future*, contains: The Inheritance of Disease, by Paul A. Lewis; Some Aspects of the Biology of Human Populations, by Raymond Pearl; The Mingling of Races, by Charles B. Davenport; The Purposive Improvement of the Human Race, by Edwin Grant Conklin; and The Intentional Shaping of Human Opinion, by H. A. Overstreet. There is a complete Index.

The plan and conception of this book is a splendid one. Its theme is Human Life. It reflects the changing philosophy of our times, and presents the newer knowledge upon which we may build a new and practical working philosophy of life. Based on the knowledge that man has evolved from animal ancestors, and is an animal himself, with definite limitations and possibilities, a reasonable and logical reaction to the knowledge is to be found in the idea that the direction of human evolution may be controlled. Studies in human biology have now come into their proper field, in the application of biological knowledge to the progress and the welfare of man himself. Ancient superstitions and conventional religious formalism are now giving place to a new conception of human life. In the knowledge we have acquired of human biology there may be found all the requisites for a new creed of life which we may designate as a biohumanistic philosophy. No

longer to be considered as a purely theoretic science, biology today may be regarded as one of the "applied sciences." The needs and problems of daily life find an answer in the biologic knowledge that has now come to have an exact basis. The proper study of mankind has now actually become that of man himself as an animal, and this means much as far as the welfare of the race is concerned. The present volume presents, neecssarily in a somewhat sketchy manner, a synopsis of our present biological knowledge of man. There is naturally a certain unevenness of treatment, with some slight overlapping, as is inevitable in composite treatises of this kind. Nevertheless the general principles are all here, and though one might wish that certain aspects of human biology might have been more adequately treated, the general result is most excellent. This reviewer believes that it is an important book which should be thoughtfully read by every educated man and woman in the country. Even if not a perfect biological bible for the human race, it is a step towards that desideratum. It offers the basic material upon which a new philosophy of life may be constructed.

Peptic Ulcer. By JACOB BUCKSTEIN, M.D. Annals of Roentgenology. A Series of Monographic Atlases. Edited by James T. Case, M.D. With Introduction by H. E. Santee, M.D. Volume X. 337 pages, 287 figures. Paul B. Hoeber, Inc., New York, 1930. Price, $12.00.

This series of monographic atlases is intended to bring to the roentgenologist at home a postgraduate course made up of the experience of leading authorities in special fields of x-ray diagnosis. It is a diagnostic guide built upon the experience of these men, and offers an invaluable series of master roentgenograms which may be studied at home and which can be compared as often as desired. The author has availed himself of the very rich material at Bellevue Hospital, where most of the roentgenograms reproduced in the monograph were obtained, and where unusual opportunities existed for the correlation of the roentgenological, clinical, surgical and pathological aspects of the subject. Representative cases have been chosen out of this very abundant material. The author portrays graphically by means of roentgenologic studies the pathologic anatomy of gastric and duodenal ulcer. A chapter on gastrojejunal ulcer and gastrojejunocolic fistulae is added, and will prove to be of great interest to the surgeon. The results of the author's study are beautifully illustrated in the systematic presentation of the subject in this volume, giving a very comprehensive view of all phases of gastric and duodenal ulcer. The book is beautifully printed, and the illustrations are excellent. It presents the subject naturally chiefly from the roentgenologic angle, the broader clinical and pathologic aspects of peptic ulcer are but briefly indicated.

Surgery at the New York Hospital One Hundred Years Ago. By EUGENE H. POOL and FRANK J. MCGOWAN. 188 pages, 24 full-page plates. Paul B. Hoeber, Inc., New York, 1929. Price in cloth, $3.00; Special Edition on Kelmscott Handmade Paper, with Illustrations on Japanese Vellum, $15.00.

This is a reprint, with additions and corrections from the Annals of Medical History, N.S. Vol. I, No. 5, 1929. It is an extremely interesting study made by Dr. Pool and Dr. McGowan of the century old records of the New York Hospital; and is especially timely in its publication, as the plans for the new building of the institution are in process of being realized. This review shows the great position which this Hospital has held since its foundation in 1771, both in the treatment of the sick and in the education of the medical profession. It played a great rôle in the early days of American medicine, particularly in the development of American surgery. At one time this Hospital may truthfully have been said to be "the great school of surgery of the whole country." It was the first hospital in the colony of New York, and the second in America. In 1791 the medical staff became a medical faculty, and was organized for clinical lectures, and the general instruction of medical students. The first attending physician was Samuel Bard (1774); and Thomas Jones was the first attending surgeon (1792). Recently a note

book, the Surgical Register, was found, which covers the period 1808-1833. From this record there can be obtained a wealth of detailed information regarding the practice of surgery one hundred years ago. The case reports contain excellent clinical descriptions. Scientific medicine was unknown; there was no bacteriology, and no conception of asepsis. The treatment of the times was purely empirical. Great potency was ascribed to drugs. No clinical thermometer was available, there was no stethoscope, no auscultation, and no nurses to assist in the treatment. Anesthesia was lacking. Yet in spite of these deficiencies, which to us today would seem to be insuperable handicaps operations of major importance were undertaken and often successfully carried out. In the notes are included descriptions of operations for aneurism, excision of cancers, amputations and plastic operations. Judged by our present standards the surgery of one hundred years ago was exceedingly primitive and restricted; and medical knowledge was extremely limited. Yet Pott wrote in 1777: "No man, however slightly acquainted with the history of Surgery, can have the smallest doubt of the superiority which its present state justly claims over that of our predecessors. . . . The surgery of the last century was coarse and cruel, painful and tedious. To simplify the art has been the aim of all the best practitioners of later times." In the "Surgical Register" there are notes on 125 cases with autopsy records. Efforts were always made to secure an autopsy after death. In many cases permission was obtained, and a satisfactory statement of the findings is given. These old case records are extremely interesting, naive and often amusing. Nothing could better illustrate the medical and surgical progress made in the last one hundred years. Their perusal is both instructive and entertaining. The volume is illustrated with pictures of the most famous of the hospital's early surgeons, and on the page opposite each illustration is a short biography. It is beautifully printed, and makes most interesting reading.

Treatment in General Practice. By HARRY BECKMAN, M.D., Professor of Pharmacology at Marquette University, Milwaukee, Wisconsin. Octavo volume of 899 pages. W. B. Saunders Company, Philadelphia and London, 1930. Price in cloth, $10.00.

The author's expressed intention in the writing of this book is "to shake the false foundations of the therapeutic credo acquired by the average young practitioner of today, which contains but two articles: one, that there are certain therapeutic principles that invariably hold and that they need only to be varied in detail in the handling of particular diseases; and the other, that the art of treatment is one that "comes" if only one has mastered the art of diagnosis." And this point of view the author believes to be the result of the neglect of thorough and painstaking teaching of therapeutics in this country. In his book the author attempts to give a remedy for this lack by the presentation of each of the principal diseases of man, exclusive of those that by prescriptive right belong within the domain of the legitimate specialties, with a description of its own peculiar therapy, as that therapy has been evolved out of the experiences of physicians all over the world. Whenever possible he has presented their work in their own words, but often it has been necessary to abstract and condense, and not infrequently to alter. The contents of the book range, therefore, from Ainhum to Yellow Fever. It is divided into sections: Infectious Diseases; Diseases Caused by Flukes; Diseases Caused by Worms; Diseases of Allergy; Deficiency Diseases; Diseases of Metabolism; Diseases of the Gastro-intestinal Tract; Diseases of the Respiratory Tract; Kidneys; Blood-forming Organs; Circulating System; Thyroid Gland; Genito-urinary Infections and Stone; Nervous System; Skin; Opium and Cocaine Addiction; Acute Poisoning; Burns; Obstetrics and Miscellaneous.

College News Notes

REPORT OF MEETING
of the
BOARD OF REGENTS

Philadelphia, Pa.
May 4, 1930

The Board of Regents of the American College of Physicians met at the College Headquarters in Philadelphia on May 4. President Sydney R. Miller presided.

The following were present: Drs. Sydney R. Miller, Arthur R. Elliott, Clement R. Jones, John A. Lichty, James S. McLester, J. C. Meakins, James H. Means, John H. Musser, O. H. Perry Pepper, George Morris Piersol, Maurice C. Pincoffs, W. Blair Stewart, Aldred Scott Warthin, S. Marx White, and Mr. E. R. Loveland, Executive Secretary.

President Miller spoke briefly about the work of the College and the plans of his administration. He mentioned the fact that he and the Executive Secretary, Mr. Loveland, had attended the annual meeting of the North Carolina Medical Association at Pinehurst on April 29, where Dr. L. B. McBrayer (Fellow), Secretary-Treasurer of that organization, and Dr. C. H. Cocke (Fellow), the College Governor for North Carolina, had arranged an informal sectional meeting of the Fellows of the College in North Carolina. In addition to addressing the general session of the North Carolina Medical Association, President Miller spoke at the luncheon of the College members, and all had an opportunity of meeting one another and discussing the College in general. President Miller recommended such sectional meetings as very valuable, and expressed the hope that during the meeting of other state societies, such group meetings of members of the College might also be arranged.

The Executive Secretary reported the following deaths since the last meeting of the Board of Regents:

Dr. W. M. Barton (Fellow), Washington, D.C.
Dr. J. Watson Campbell (Fellow), Halstead, Kans.
Dr. James D. Love (Fellow and Governor for Florida), Jacksonville, Fla.
Dr. Philip S. Roy (Fellow), Washington, D.C.
Dr. Edward V. Silver (Fellow), New York, N.Y.
Dr. Garnett Nelson (Fellow), Richmond, Va.
Dr. George F. Roberts (Fellow), Salt Lake City, Utah.

The Board of Regents accepted the resignations of Dr. Robert A. Oden (Associate), Washington, D.C., and of Dr. Herbert G. Wertheimer (Associate), Pittsburgh, Pa.

Several cases of reduction or remission of dues, because of disability, were acted upon. The following resolution was regularly adopted:

RESOLVED, That the Board of Regents authorize a reduction in the annual dues of Associates engaged in full-time medical teaching, purely scientific research, the Public Service, etc., to $10.00 per annum, the same as provided for Fellows.

In accordance with the By-Laws, Article XIII, Secton 2, the following names were dropped from the rolls of the College, as of April 1, 1930:

ARKANSAS
Dr. Thomas Scott Jordan, Taylor (Associate)
DISTRICT OF COLUMBIA
Dr. Edward W. Burch, Washington (Associate)
ILLINOIS
Dr. Petra M. Dahl, Chicago (Associate)
KENTUCKY
Dr. R. Hayes Davis, Louisvlle (Associate)
MICHIGAN
Dr. Bruce C. Lockwood, Detroit (Fellow)
Dr. H. D. Knapp, Flint (Associate)
MISSOURI
Dr. Drew Luten, St. Louis (Fellow)
Dr. C. G. Conover, Kansas City (Associate)
Dr. Harry L. Jones, Kansas City (Associate)
NEBRASKA
Dr. Edmund George Zimmerer, Lincoln (Fellow)
NEW JERSEY
Dr. Raphael Gilady, Hackensack (Associate)
NEW YORK
Dr. J. Francis Ward, Brooklyn (Associate)
OHIO
Dr. Orville J. Walker, Youngstown (Fellow)
Dr. C. A. Craig, Cambridge (Associate)
Dr. Ellery P. Edwards, Cleveland (Associate)
Dr. G. B. Fliedner, Cleveland (Associate)
PENNSYLVANIA
Dr. D. H. Parmet, Allentown (Associate)
Dr. Thomas G. Simonton, Pittsburgh (Associate)
TENNESSEE
Dr. W. T. Swink, Memphis (Fellow)
UTAH
Dr. T. Catlett Gibson, Salt Lake City (Fellow)
WEST VIRGINIA
Dr. Dorsy M. Ryan, Hinton (Associate)
CANADA
Dr. J. I. Ferguson, London, Ont. (Fellow)
Dr. J. D. Adamson, Winnipeg, Man. (Associate)

The Executive Secretary reported upon the receipt of gifts to the College Library of publications by members. The names and titles of reprints and books have already been published in these columns from month to month.

The Executive Secretary reported an additional new Life Member, Dr. Frederick R. Barnes, Fall River, Mass., who subscribed in full to the Life Membership Fund on April 22, 1930.

The Executive Secretary presented attendance reports and financial statements of the Minneapolis Clinical Session conducted during February, 1930.

Dr. J. C. Meakins, Chairman of the Committee on the John Phillips Memorial, presented the following report

May 3, 1930.

"To the PRESIDENT
AMERICAN COLLEGE OF PHYSICIANS:

Sir:

The Committee appointed by you March 12, 1930, to draw up rules governing the awarding of the JOHN PHILLIPS MEMORIAL PRIZE begs to report as follows:

The Committee met on one occasion, May 3, at 2:30 o'clock in the rooms of the College and adopted the following regulations:

The Committee would recommend:

I. Interpretation of Internal Medicine—This term should include not only Clinical Science, but, in addition, all those subjects which have a direct bearing upon the advancement of Clinical Science;

II. (a) That not less than two or more than three members of the Committee would be reappointed each year;

(2) That the Prize be publicly advertised, and announce that the dissertations of candidates should be mailed to the Executive Secretary not later than August 31 of each year. The dissertation may be based upon either published or unpublished original work.

(c) Form of announcement:

The American College of Physicians announces the JOHN PHILLIPS MEMORIAL PRIZE of $1,500.00 is to be awarded for the most meritorious contribution in Internal Medicine and sciences contributing thereto under the following conditions:

(1) The contribution must be submitted in the form of a thesis or dissertation based upon published or unpublished original work.

(2) It must be mailed to the Executive Secretary of the American College of Physicians on or before August 31.

(3) The thesis or dissertation must be in the English language, in triplicate, in typewritten or printed form, and the work upon which it is based must have been done in whole or in part in the United States or Canada.

(4) The recipient of the prize would be expected to read the essay at the next Annual Meeting of the College after which he would be officially presented with the prize by the President.

(5) The College reserves the right to make no award of the prize if a sufficiently meritorious piece of work has not been received.

(6) The announcement of the Prizewinner will be made not later than two months before the Annual Meeting.

III. The Committee should inform the President of the name of the recipient of the prize at least two months before the date of the Annual Meeting.

IV. The Committee recommends that the Executive Secretary inform the recipient of the Prize that the College would be pleased to defray his transportation expenses when he attends the Annual Meeting to receive the prize.

Respectfully,

(Signed) J. C. Meakins
Chairman"

The following resolution was regularly adopted:

RESOLVED, That the above report of the Committee on the John Phillips Memorial be adopted in full by the Board of Regents.

Dr. Arthur R. Elliott, who had acted as Chairman of this Committee during the Minneapolis Clinical Session, reported fully upon the work previously accomplished.

The following resolution was regularly adopted:

RESOLVED, That the Editor and Executive Secretary be instructed to prepare a suitable announcement to be entered in the June Issue of ANNALS OF INTERNAL MEDICINE, and that the President write an appropriate letter to Mrs. Phillips concerning the final plan adopted by the Board of Regents, for the Phillips Memorial.

Upon recommendation of the Committee on Credentials, as presented by Dr. George Morris Piersol, Chairman, a resolution was adopted providing for the election of the following candidates to Fellowship in the College:

Glaister Herod Ashley.....Denver, Colo.
Joseph T. Beardwood, Jr.....Philadelphia, Pa.
William S. Collier.....Trenton, N. J.
Alexander T. Cooper.....Denver, Colo.
Alva Brown Craddock.....Asheville, N. C.
George Blaine Crow .....Burlington, Iowa
Kallman Meyer Davidson.....Boston, Mass.
Ernest Speers duBray.....San Francisco, Calif.
James Nicholas Dunn.....St. Paul, Minn.
Lee Pettit Gay.....St. Louis, Mo.
Robert Finley Gayle, Jr.....Richmond, Va.
Daniel Johnson Glomset.....Des Moines, Iowa
John W. Gray.....Newark, N. J.
Henry Spencer Houghton.....Iowa City, Iowa
Thomas Klein.....Philadelphia, Pa.
Christian Bateman Luginbuhl.....Des Moines, Iowa
Arthur Clayton McCarty.....Louisville, Ky.
T. Grier Miller.....Philadelphia, Pa.
Seeley Greenleaf Mudd.....Los Angeles, Calif.
Marcus Ward Newcomb.....Browns Mills, N. J.
William Crane Nichols.....Fargo, N. D.
John H. Peck.....Des Moines, Iowa
Florence Polk.....Philadelphia, Pa.
James Manara Rector.....Columbus, Ohio
Clifford Phillip Rutledge.....Shreveport, La.
Samuel Lyon Salasin.....Atlantic City, N. J.
Albert Bernard Siewers.....Syracuse, N. Y.
Fred M. Smith.....Iowa City, Iowa
James Shirley Sweeney.....Dallas, Texas
Fresenius Van Nuys.....Weston, Mass.
Harry David Williams.....Trenton, N. J.

President Miller reported upon the advance arrangements made by himself, Dr. Pincoffs, General Chairman, and Mr. Loveland, Executive Secretary, for the Fifteenth Annual Clinical Session to be held at Baltimore, Maryland, March 23-27, 1931. The Alcazar, a very suitable Convention Auditorium, with adequate exhibit and registration space, has been engaged. The Lord Baltimore Hotel, the largest and newest hotel in the City, has been engaged for hotel headquarters.

The Executive Secretary reported that he had underway the publication of the 1930 Supplement to the College Directory. The regular Directory of the College is printed completely every two years, with a Supplement of new members printed during the intervening year.

President Miller reported that two vacancies on the Board of Governors were outstanding, the first for the State of Florida, due to the death of Dr. James D. Love; and the second for the State of Connecticut, due to the voluntary resignation of Dr. Oliver T. Osborne, on account of ill health. After consultation with Dr. Stewart, Chairman of the Board of Governors, and in accordance with the provisions of the By-Laws, President Miller, therefore, appointed Dr. Turner Z. Cason, of Jacksonville, for the State of Florida, and Dr. Henry F. Stoll, of Hartford, for the State of Connecticut, both to serve until the next regular election at the Baltimore Session.

Dr. W. Blair Stewart, Chairman of the Board of Governors, in accordance with the resolution adopted at the last meeting of the Board of Governors at Minneapolis, February 14, appointed the following members to the Committee on Credentials for Associateship:

Allen A. Jones, Buffalo, N. Y., *Chairman*
Charles H. Cocke, Asheville, N. C., *Vice Chairman*
Egerton L. Crispin, Los Angeles, Calif.
E. J. G. Beardsley, Philadelphia, Pa.
Ernest B. Bradley, Lexington, Ky.

Dr. Stewart suggested the desirability and advisability of having an annual luncheon, or get-together meeting, of the Fellows of the American College of Physicians during the Detroit meeting of the American Medical Association, in the belief that this would be beneficial in advancing the interests of the College, and in giving its members an opportunity to meet together and get better acquainted.

Dr. Lewis J. Moorman (Fellow), Oklahoma City, Okla., was one of the guest speakers at the 55th annual session of the Arkansas Medical Society at Fort Smith, May 6-8. His subject was "More Recent Therapeutic Measures Employed in the Treatment of Tuberculosis."

Dr. Charles W. Duval (Fellow), New Orleans, La., was guest of honor at the 57th annual meeting of the Florida Medical Association, held at Pensacola, May 6-7. He delivered an address on "Correlation of Urinary Findings and Renal Pathology in Experimental Streptococcal Nephritis."

Dr. Logan Clendening (Fellow), Kansas City, Mo., delivered an address on "Physical Diagnosis" before the annual meeting of the Illinois State Medical Society at Joliet, May 20-22.

Dr. Martin E. Rehfuss (Fellow), Philadelphia, delivered the oration in medicine before the Illinois State Medical Society at Joliet, May 20-22, on "Medicine of the Future—What Can We Expect."

Dr. David J. Davis (Fellow), Wilmette, Ill., was one of the speakers at the symposium on septic sore throat featured by a joint meeting of the Milk Commission and the Chicago Medical Society on April 30.

Dr. Fred M. Smith (Fellow), Iowa City, Iowa, addressed the Chicago Society of Internal Medicine, April 28, on "Reflex Gastric Pain."

Under the Presidency of Dr. John H. Peck (Fellow), Des Moines, Iowa, the 79th annual meeting of the Iowa State Medical Society was held at Marshalltown, May 14-16. The address in medicine was given by Dr. O. H. Perry Pepper Fellow), Philadelphia; his subject being "The Internist's Responsibility for the Fruitless Laparotomy." Dr. William Gerry Morgan (Fellow), President-Elect of the American Medical Association, was a guest speaker, and

spoke on "Functional Diseases of the Alimentary Tract."

Dr. William C. Menninger (Fellow), Topeka, Kans., delivered an address before the annual meeting of the Kansas Medical Society, May 6-8, on "Mental Disturbances Associated with Puerperium."

Dr. James Alex. Miller (Fellow), New York, N. Y., was one of the speakers on a symposium on tuberculosis conducted before the April 30 meeting of the Greater New York Public Health Officers' Association.

Dr. Allan C. Eustis (Fellow), New Orleans, La., and Dr. Seale Harris (Fellow), Birmingham, Ala., were guest speakers at the 64th annual session of the State Medical Association of Texas, May 6-8. Their subjects were "Diagnosis and Treatment of Liver Dysfunction" and "Cure of the Ulcer Patient,' respectively.

The following Fellows of the College will deliver addresses before the American Association for the Study of Goiter at Seattle, July 10-11:

Dr. Lewis M. Hurxthal, Boston, Mass., Cardiovascular System in Goiter."

Dr. Oliver P. Kimball, Cleveland, Ohio, "Relation of Endemic Goiter to Mental Efficiency."

Dr. Anders Frick (Fellow), Chicago, Ill., recently addressed the Elkhart County Medical Society (Indiana) on "Management of Peptic Ulcer."

Dr. Harold F. Dunlap (Associate), Rochester, Minn., addressed the Madison County Medical Society, April 15, on "Differential Diagnosis of Hyperthyroidism and Some of Its Atypical Manifestations."

Dr. James S. McLester (Fellow), Birmingham, Ala., and Dr. John H. Musser (Fellow), New Orleans, La., addressed the Mississippi State Medical Association at Vicksburg, May 13-15, on "Cardiac and Other Disabilities of Advancing Years" and "Observations on Gastro-Intestinal Disease," respectively.

Dr. James E. Talley (Fellow), Professor of Cardiology at the Graduate School of Medicine of the University of Pennsylvania, was recently elected President of the Philadelphia Heart Association, succeeding Dr. Henry K. Mohler (Fellow), Philadelphia.

Dr. William Gerry Morgan (Fellow), Washington, D. C., was a guest speaker at the meeting of the South Carolina Medical Association, May 6-8.

Dr. Horton R. Casparis (Fellow), Nashville, Tenn., recently addressed the Gibson County Medical Society on "Tuberculosis in Children."

Dr. W. McKim Marriott (Fellow), Dean and Professor of Pediatrics, Washington University School of Medicine, delivered a course of lectures before the San Diego Academy of Medicine, May 5-6. Dr. Marriott also was a guest speaker at the annual meeting of the California Medical Association, held at Del Monte, April 28-May 1.

The following Fellows of the College were on the program of the April meeting of the Homeopathic Medical Society of the County of Philadelphia, held on April 10, at the Hotel Pennsylvania:

Dr. E. Roland Snader, Jr., "Metabolic Phenomena of Hyper- and Hypothyroidism."

Dr. G. Morris Golden, "Non-Surgical Therapy of Hyper- and Hypothyroidism."

Dr. Arthur U. Desjardins (Fellow), Rochester, Minn., was one of the guest speakers at the annual meeting of the California Medical Association, held at Del Monte, April 28-May 1. He delivered an address on "Value of Radiotherapy in Mediastinal Tumors."

Dr. Walter C. Alvarez (Fellow), Rochester, Minn., recently addressed the

Louisiana State Medical Society on "Puzzling Types of Indigestion."

Dr. Francis E. Harrington (Fellow), Minneapolis, was the recipient of a dinner marking the tenth year of his service as City Health Commissioner.

Dr. Linn J. Boyd (Fellow), New York, is author of an article, "Chronic Arthritis," which appeared in the April issue of the Journal of the American Institute of Homeopathy.

Dr. Leonard G. Rowntree (Fellow), Rochester, Minn., and Dr. Cyrus C. Sturgis (Fellow), Ann Arbor, Mich., delivered addresses before the Ohio State Medical Association held at Columbus, May 13-15, on "Results of Sympathetic Ganglionectomy and Ramisectomy in Treatment of Chronic Arthritis" and "Appraisal of Therapeutic Measures Used in Treatment of the Anemias," respectively.

Dr. George E. Pfahler (Fellow), Philadelphia, Pa., was a speaker at the afternoon session of the cancer control meeting of the Philadelphia County Medical Society on April 23.

Dr. G. Morris Golden (Fellow), Philadelphia, Pa., is author of an article, "Deductions from Studies of Blood Pressure and Pulse Rate and Their Significance from the Standpoint of the General Practitioner," which appeared in the April Issue of the Journal of the American Institute of Homeopathy.

Dr. O. H. Perry Pepper (Fellow), Philadelphia, was a guest speaker at the Graduate Clinic for Physicians in Virginia, sponsored by the Richmond Academy of Medicine, on April 22.

Dr. Clarence A. Smith (Fellow), Seattle, recently delivered an address before the King County Medical Society on Galvanic Therapy.

The above Society is sponsoring a Graduate Medical Course at the Washington University, July 14-15. Among the lecturers will be Dr. Thomas Addis (Fellow), San Francisco, Calif.

The following Fellows of the College were guest speakers at the 63rd annual meeting of the Medical Association of the State of Alabama, at Montgomery, April 15-18:

Dr. Paul H. Ringer, Asheville, N. C., "Diagnosis and Rest: Two Essentials in Overcoming Pulmonary Tuberculosis."

Dr. Noel C. Womack, Jackson, Miss., "Secondary Anemias in Children."

The 39th annual meeting of the Arizona State Medical Association was held at Phoenix, April 24-26, under the Presidency of Dr. Samuel H. Watson (Fellow), Tucson. A symposium on the chest was presented by Dr. Allen W. Krause (Fellow), Tucson; Dr. Charles S. Kibler (Fellow), Tucson; and Dr. Watson.

Dr. F. M. Pottenger (Fellow), Monrovia, Calif., was one of the speakers at the Saturday session. His subject was "The Nature of Symptoms."

Dr. L. F. Barker (Fellow), Baltimore, Md., delivered the first course of lectures under the Porter Lectureship in Medicine of the University of Kansas School of Medicine, April 1-2, at the Bell Memorial Hospital. The subjects of the lectures were "Diagnosis and Treatment of the Commoner Personal Disorders," and "Psychology and Medicine."

Dr. Henry R. M. Landis (Fellow), Philadelphia, Pa., recently addressed the Wayne County Medical Society on "Tuberculosis."

Dr. Arthur L. Smith (Fellow), Lincoln, Nebr., recently gave an illustrated address on "Tachycardia" before the Dawson County Medical Society.

Dr. Carl V. Vischer (Fellow), Philadelphia, Pa., read "A Survey of the Progress in Internal Medicine, 1929" at the Conference of the St. Luke's Hospital Staff, April 16.

Dr. Howard T. Karsner (Fellow), Cleveland, Ohio, addressed the Toledo Academy of Medicine, April 4, on "Primary Carcinoma of the Lung."

Dr. Stewart R. Roberts (Fellow), Atlanta, Ga., was a guest of the staff of the Pittsburgh Diagnostic Clinic, April 30, and delivered a lecture on "The Gallbladder-Heart Problem."

Among Fellows of the College who participated in the annual clinic of the Dallas Southern Clinical Society, April 14-18, were:

Dr. Alexander B. Moore, Rochester, Minn.
Dr. Logan Clendening, Kansas City, Mo.
Dr. Cyrus C. Sturgis, Ann Arbor, Mich.

Dr. John C. Thompson (Fellow), Lincoln, Nebr., is the author of an article on "Electrocardiographic Interpretation," which appeared in the May Issue of the Nebraska State Medical Journal.

Dr. Seale Harris, Jr. (Associate), Birmingham, Ala., is the author of an article on "Jamaica Ginger Paralysis (A Peripheral Polyneuritis)," which appeared in the May Issue of the Southern Medical Journal.

Dr. Clarence M. Trippe (Fellow), Asbury Park, N. J., is recovering from an attack of encephalitis lethargica.

Dr. Lorena M. Breed (Fellow), Pasadena, Calif., will soon leave for a fourth trip around the world, visiting various points in Europe, enroute to Haidarabad, Deccan, India (the largest native state in India), where she formerly had charge of a hospital for eleven years.

Dr. B. S. Pollak (Fellow), Secaucus, N. J., addressed the New Jersey State Hospital Association on May 22 on "The Necessity of Caring for the Tuberculous in the General Hospital." On May 23, he addressed the New Jersey Tuberculosis League on "Our Present Concept of Tuberculosis in Childhood."

Dr. Oliver T. Osborne (Fellow), New Haven, Conn., was recently elected to Honorary Fellowship in the American Stomatological Association, and in consideration of his distinguished service to medicine, he was re-elected Honorary Vice President.

Dr. Osborne also was recently elected to Honorary Fellowship in the American Society of Stomatologists with the preamble, "For your contribution to the advancement of the science of stomatology and the cause of dentistry as a specialty of medicine in America."

Dr. Osborne is the author of an article on "Pharmaceutical Advertisements" in the April, 1930, Number of the "Medical Mentor."

Dr. Lee A. Riely (Fellow), Oklahoma City, Okla., is the author of an article on "Tularemia," which appeared in the March Issue of the Journal of the Oklahoma State Medical Association.

In the same issue, Dr. T. H. McCarley (Fellow), McAlester, Okla., had an article entitled, "Primary Repair of the Cervix Uteri Lacerated in Labor."

Dr. J. A. Myers (Fellow), Minneapolis, Minn., on April 5 attended the meeting of the Central Clinical Research Club of St. Louis. The program was arranged by the faculty of the St. Louis University Medical School and the Washington University Medical School.

On April 7 and 8, Dr. Myers addressed the County Medical Society of Oklahoma City and the faculty of the Oklahoma Medical School. On May 10, he addressed the National Tuberculosis Association in Memphis, and on May 12, delivered a paper before a clinical group in Lincoln, Nebr., at the opening of the new wing of the Bryan Memorial Hospital. On the same evening, he addressed the joint meeting of the Nebraska Medical Association and the Nebraska Tuberculosis Association.

Dr. F. M. Pottenger (Fellow), Monrovia, Calif., gave an address on "How May a General Practitioner Diagnose Tuberculosis" at the third annual spring Clinical

Conference of the Dallas Southern Clinical Society, April 15.

On the day previous, April 14, he gave a clinic on "Treatment of Tuberculosis" at the Parkland Hospital, Dallas, and on the morning of April 15, he gave another clinic on "Diagnosis of Tuberculosis" at the Methodist Hospital of the same City.

Dr. Ross V. Patterson (Fellow), Philadelphia, Dean of the Jefferson Medical College, is President-Elect of the Medical Society of the State of Pennsylvania. On April 29, he delivered an address before the annual meeting of the North Carolina State Medical Association.

Dr. William Devitt (Fellow), Allenwood, Pa., was the chief speaker at a public health night meeting under the auspices of the Philadelphia County Medical Society, recently. Dr. Arthur C. Morgan (Fellow), Philadelphia, Pa., presided at the meeting.

Dr. Judson Daland (Fellow), Philadelphia, was one of the chief speakers at a joint meeting of the Montgomery County Medical Society and the Montgomery County Dental Society on March 5.

Dr. Emanuel Libman (Fellow), New York, N. Y., will be a guest speaker on the program for the section on medicine at the Johnstown meeting of the Medical Society of the State of Pennsylvania.

In the April Issue of the American Journal of the Medical Sciences, the following papers by Fellows of the College were published:

Dr. David P. Barr, St. Louis, Mo., "The Clinical Syndrome of Hyperparathyroidism."

Dr. Lewis M. Hurxthal, Boston, Mass., "Auricular Fibrillation in Patients with Goiter."

Dr. Philip B. Matz, Washington, D. C., "A Study of Intestinal Tuberculosis Among Ex-service Men."

Dr. Henry W. Woltman, Rochester, Minn., "Pressure as a Factor in the Development of Neuritis of the Ulnar and Common Peroneal Nerves in Bedridden Patients."

Dr. James J. Waring (Fellow), Denver, Colo., was elected President of the Denver Tuberculosis Association on April 15.

Under the Presidency of Dr. William R. Dancy (Fellow), Savannah, the Medical Association of Georgia held its 81st annual session at Augusta, May 14-16.

Dr. I. Seth Hirsch (Fellow), New York, addressed the Chicago Roentgen Ray Society on May 8, giving a "Eulogy of Roentgen."

Dr. Arlie R. Barnes (Fellow), Rochester, Minn., addressed the Tippecanoe County Medical Society of Indiana, May 8, on "Heart Disturbances."

Dr. Estes Nichols (Fellow), Portland, gave a paper on "Early Treatment of Tuberculosis" before the Kennebec County Medical Society, April 22.

Dr. Thomas J. Burrage (Associate), Portland, addressed the 78th annual session of the Maine Medical Association, June 2-4, on "Angina Pectoris and Acute Coronary Occlusion."

Dr. William Gerry Morgan (Fellow), Washington, D. C., spoke at the banquet on "Functional Diseases of the Alimentary Tract."

Dr. Emanuel Libman (Fellow), New York, last year endowed the Hideyo Noguchi Lectureship in the History of Medicine. The first course in the Lectureship was given May 8-10 by Dr. Charles Singer of the University College, London, his general subject being "The Transition from Medieval to Modern Science."

Dr. Guy L. Kiefer (Fellow), State Health Commissioner for Michigan, addressed the fifth annual meeting of the Michigan Association of Industrial Physicians and Surgeons on the subject, "Health Education in Industry," April 25.

Dr. Frank Smithies (Master), Chicago, spoke on "Diagnosis and Treatment of Gastro-Enterological Cases in General Practice" during the graduate conference and clinic sponsored by the Ingham County Medical Society and the Michigan State Medical Association, recently.

The Nebraska State Medical Association held its sixty-second annual convention at Lincoln, May 13-15. The third annual health week, May 11-17, was held in conjunction with the state medical sessions, the meetings being held in clubs and churches. The following Fellows of the College were on the program to give health messages to the laity:

Dr. A. D. Dunn, Omaha, "Some Remarks on Choosing a Doctor."

Dr. George N. Neuhaus, Omaha, "Path of Happiness."

Dr. George L. Pinney, Hastings, "Exercise and Rest."

Dr. Francis W. Heagey, Omaha, "Responsibility of a College Graduate in the Health Program of the Community."

Dr. Samuel A. Levine (Fellow), Boston, was a guest speaker at the one hundred and twenty-fourth annual meeting of the Medical Society of the State of New York at Rochester, June 2-4, his subject being "Can This Heart Stand an Operation."

Dr. Levine also addressed the Philadelphia Heart Association, May 7, on "Clinical Conception of the Development of Rheumatic Heart Disease."

Dr. Elmer L. Eggleston (Fellow), Battle Creek, Mich., addressed the Sixth Councilor District of the Medical Society of the State of Pennsylvania and the Pennsylvania Radiological Society at Huntington, May 15, on "Intestinal Problems Frequently Encountered by the Internist."

Dr. Daniel J. McCarthy (Fellow), Philadelphia, spoke before the Cambria County (Pennsylvania) Medical Society, May 8, on "Fat and Blood."

Dr. Orlando H. Petty (Fellow), Philadelphia, presented a paper on diabetes mellitus before the annual meeting of the Eleventh Councilor District of the Pennsylvania State Medical Society, June 12.

Dr. J. W. Torbett (a Fellow) of Marlin, Texas, read an article before the Texas State Medical Association at its recent meeting in Mineral Wells on "The Classification, Diagnosis and Treatment of Arthritis."

Dr. Adolph H. Nahman (Fellow), wife and family, of San Francisco, Calif., sailed from New York on May 15 for Europe. Their itinerary includes Germany, Czechoslovakia, Austria, Italy, Switzerland, France, Poland, Russia and the British Isles. While abroad, Dr. Nahman will visit the many European clinics. He expects to return to San Francisco about August 22.

Dr. A. H. Waterman (Fellow), Chicago, addressed the Hancock (Ohio) County Medical Society on April 17, his subject being, "The Importance of a Diagnostic Survey."

Dr. Sidney A. Portis (Fellow), Chicago, Professor of Medicine at Loyola University School of Medicine, delivered a medical clinic at St. Mary's Hospital, Quincy, Illinois, May 12. Dr. Portis discussed and showed cases of Chronic Peptic Ulcer, Ulcerative Colitis and Thyrotoxicosis.

Dr. Warren F. Pearce (Fellow), Quincy, had charge of the Clinic.

At the seventy-seventh annual session of the Medical Society of the State of North Carolina at Pinehurst, April 28, 29 and 30, the following Fellows contributed papers, as indicated:

Dr. Allen H. Bunce, Atlanta, Ga., "Opportunity and Responsibility of Organized

Medicine in connection with the so-called High Cost of Medical Care."

Dr. William DeB. McNider, Chapel Hill, N. C., "The Correlation of Observations made in Studies of Experimental Nephritis with Certain Clinical Conditions."

Dr. C. T. Smith and Dr. W. Bernard Kinlaw, Rocky Mount, N. C., "The Clinical Consideration of an Anemia of Pregnancy and the Puerperium."

Dr. Ross V. Patterson, Dean, Jefferson Medical College of Philadelphia, "Occlusion of the Coronary Artery."

Dr. P. P. McCain, Sanatorium, N. C., discussion, "The Importance of an Early Diagnosis in the Treatment of the more common Chest Conditions" and "Tuberculosis Empyema: Treatment by a Combination of Irrigation and Suction with Aseptic Paravertebral Thoracoplasty."

Dr. L. B. McBrayer, Southern Pines, N. C., "Tuberculosis Control Applied to a North Carolina County."

Among Fellows of the College who addressed the forty-ninth annual session of the South Dakota State Medical Association at Sioux Falls, on May 20-22, were the following:

Dr. Moses Barron, Minneapolis;

Dr. Edward L. Tuohy, Duluth, "Chronic Nontuberculous Lung Lesions";

Dr. Ernest E. Irons, Chicago, "Some Factors in the Diagnosis and Treatment of Chronic Arthritis."

Dr. James B. McElroy (Fellow), Memphis, was elected President of the Tennessee State Medical Association at its annual meeting at Nashville on April 10.

At the meeting of the American Association of Pathologists and Bacteriologists at New York on April 17-18, the following Fellows of the College were elected officers:

Dr. George R. Callender, Washington, D. C., *President.*

Dr. Ward J. MacNeal, New York, N. Y., *Vice President*

Dr. Howard T. Karsner, Cleveland, Ohio, *Secretary.*

Dr. James Z. Naurison (Fellow), Springfield, Mass., spoke before the Brookfield Medical Society, March 19, on "Diseases of the Chest, Pains, their Diagnosis and Treatment."

On May 14, Dr. Naurison delivered an address before the Windham County Medical Society in Bellows Falls, Vermont.

Dr. N. Emmons Paine (Fellow), West Newton, Mass., has recently published a book, "Thomas Payne of Salem and his Descendants." It is a carefully prepared genealogy of Thomas Payne since his emigration from England.

Dr. Crawford R. Green (Fellow), Troy, N. Y., presented a paper entitled "Leaves from a Therapeutic Note-Book" on April 22 at the meeting of the New York State Homeopathic Medical Society in Brooklyn.

The Southern Pediatric Seminar is a postgraduate summer course in methods of diagnosis, prevention, and treatment of diseases of children. It is held at Saluda, N. C.

On the program of their tenth session, July 28 to August 9, 1930, the following Fellows of the American College of Physicians are among the teachers:

Dr. Frank Howard Richardson, Black Mountain, N. C.

Dr. W. L. Funkhouser, Atlanta, Ga.

Dr. Charles J. Bloom, New Orleans, La.

Dr. Philip F. Barbour, Louisville, Ky.

Dr. Stewart H. Welch, Birmingham, Ala.

Dr. W. C. Davison, Durham, N. C.

Dr. E. A. Hines, Seneca, S. C.

Dr. Paul H. Ringer (Fellow), Asheville, N. C., is President of the Board of Medical Examiners of the State of North Carolina.

Dr. David Riesman (Fellow), Philadelphia, and Dr. Harold S. Davidson (Fellow), Atlantic City, read a paper on "Psittacosis," April 28, before the Section on General

Medicine of the College of Physicians of Philadelphia.

Dr. Walter M. Simpson (Fellow), Dayton, Ohio, is Chairman of the Essay Committee of the American Association for the Study of Goiter, which is going to award a cash prize of $300.00 annually for the best original thesis dealing with some aspect of the goiter problem.

Dr. A. S. Warthin (Master) was elected President of the American Association of Medical History at its recent meeting in Atlantic City.

Dr. C. V. Weller (Fellow) was elected Secretary of the American Association of Medical History at the Atlantic City meeting, May 14.

On Friday, May 2, Dr. Frank Smithies (Master), Chicago, held a clinic on gastro-intestinal diseases in the Amphitheater of the Long Island College Hospital. He later appeared before the Medical Society of the County of Kings, delivering one of the lectures of the Friday Afternoon Practical Lecture Course of that Society, his subject being, "Defective Liver Function as a Cause of Chronic Endogenous Skin Lesions." More than two hundred and fifty practitioners were in attendance.

That evening there was held at the Montauk Club, to do honor to Dr. Smithies, one of Brooklyn's most notable gatherings—the first get-together meeting of Brooklyn Fellows and Associates of the American College of Physicians. Of the seventy-two men appearing on the Roster, sixty attended, two were ill, five were out of town, and, therefore, only five were not accounted for. Following the dinner, Dr. Luther F. Warren, President of the Medical Society of the County of Kings, and one of Brooklyn's best known Fellows, after a few well chosen words of greeting to the honored guest and an outline of Dr. Smithies' invaluable services to the College in its early struggles, introduced as Toastmaster, Dr. Albert F. R. Andresen, who in turn introduced as speakers, Drs. LeGrand Kerr, Robert F. Ives, Thurston H. Dexter and Siegfried Block, all of whom spoke in eloquent terms of Dr. Smithies' many contributions to medicine as a whole and of his work toward advancing the College to the forefront of American medical organizations. Dr. Smithies replied with a recital of many of the intimate details connected with the early history of the College, and in closing expressed the hope that groups of Fellows in other communities might get together at intervals and have an opportunity to greet each other and to improve the spirit of the organization.

Before the closing of the meeting, the Fellows present passed a resolution to have a Committee appointed for the purpose of arranging for an annual dinner, similar to this one, which was voted to be a complete success.

Dr. Frank Bethel Cross (Fellow), Brooklyn, N. Y., recently addressed the Flatbush Medical Society on "Recent Trends in the Management of Diabetes."

Dr. Cross is a member of the party of American and Canadian physicians who left on May 23 for a tour of the French spas and therman springs as guests of the Institute of Hydrology of the College of France.

Dr. Aaron E. Parsonnet (Fellow), Newark, N. J., delivered a talk on "Coronary Thrombosis" before the Middlesex County Medical Society on April 16 at the City Hospital of Perth Amboy.

Dr. Robert M. Moore (Fellow), Indianapolis, Ind., addressed the Northern Tri-State Medical Association at Fort Wayne, April 8, on "Some Observations on Heart Disease."

Dr. Harold G. F. Edwards (Fellow), Shreveport, La., recently addressed the Tri-State Medical Society at Marshall (Texas), "On Roentgen Therapy."

The Executive Secretary of the College announces the following gifts of publications by members of the College Library:

Dr. Julius H. Comroe (Fellow), York, Pa.:

"Eczema—Its Proper Management"
"Macroglossia, Report of a Case"
"Has the Present System of Placarding Houses Proved Beneficial to the Public"
"Jaundice in Typhoid Fever—An Unusual Case"
"Prescribing versus Dispensing"
"The Use and Abuse of the Tonsils"
"A Plea for Longer Intervals in Milk-Feeding"
"A Rare Manifestation of Empyema Necessitatis"
"Preliminary Report on the Use of X-Rays in Neuritis"
"The Relationship of the Consultant to the Practitioner"
"General Principles Underlying the Treatment of Syphilis"
"Patent Thyrolingual Duct and its Affections; Report of Cases; Use of X-Rays"
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"An Unusual Case of Bradycardia"
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"What Constitutes Medical Appendicitis"

Dr. Frederic J. Farnell (Fellow), Providence, R. I.:
"Social Work and Our Institutions"
"Problems the Welfare Commission is Facing"
"Juvenile Delinquency"
"Institutional Activities"

Dr. Philip B. Matz (Fellow), Washington, D. C.:
"A Study of Intestinal Tuberculosis Among Ex-service Men"

Dr. Aaron E. Parsonnet (Fellow), Newark, N. J., with Dr. Albert S. Hyman (Fellow), New York, N. Y.:
"Herpes Zoster and Angina Pectoris"

Dr. Bernard L. Wyatt (Fellow), Tucson, Ariz.:
"Chronic Arthritis and Rheumatoid Conditions"

Dr. James W. Hunter (Fellow), Norfolk, Va.:
"The Extrasystole"

Dr. F. M. Pottenger (Fellow), Monrovia, Calif., one book:
"Symptoms of Visceral Disease"

Dr. Edwin Henes, Jr. (Fellow), Milwaukee, Wis.:
One Book, "Detroit Proceedings of the Inter-State Postgraduate Association of North America"

Dr. G. E. Holtzapple (Fellow), York, Pa.:
Six Reprints: "The Uses and Effects of Oxygen Gas and Nux Vomica in the Treatment of Pneumonia"
"Family Periodic Paralysis"
"Periodic Paralysis"
"Lodge Practice"
"Hemochromatosis with Cirrhosis of the Liver"
"Mycotic Aneurysm of the Aortic Arch, with Presentation of a Specimen"

Dr. Milo K. Tedstrom (Associate), Anaheim, Calif.:
One Reprint: "Hemochromatosis"

Dr. James Z. Naurison (Fellow), Springfield, Mass.:
One Reprint: "The Use of Non-Specific Protein Therapy in General Practice"

THE 1931 CLINICAL SESSION

The Fifteenth Annual Clinical Session of the American College of Physicians will be held in Baltimore, Maryland, March 23-27, inclusive, 1931. The hotel headquarters will be the Lord Baltimore Hotel. The headquarters for registration, exhibits and the general scientific meetings will be The Alcazar, Cathedral and Madison Streets, Baltimore.

The Alcazar is a very fine hall, seating about fifteen hundred, and so arranged that an amplifying system with loud speakers will be unnecessary. This will contribute to the ease of many speakers and will add to the enjoyment of the audience. The exhibits will be splendidly housed in the large gymnasium and ballroom, immediately adjacent to the meeting room. The Alcazar is about seven squares removed from the hotel headquarters, and may be conveniently reached by trolley, bus or taxicab. The

taxicab fare for one to five people is but twenty-five cents.

Dr. Sydney R. Miller, President of the College, has in charge the selection of speakers and subjects on the general program, while Dr. Maurice C. Pincoffs is the General Chairman of the Session and is responsible for all local arrangements, in addition to the preparation of the program of clinics and demonstrations.

PLACEMENT SERVICE

Through the Executive Offices, the College will assist its members in locating new appointments, or in obtaining assistants. The College will attempt, in all cases, to secure authentic information, but cannot assume responsibility in connection with recommendations. Address all inquiries to E. R. Loveland, Executive Secretary, 133-135 S. 36th Street, Philadelphia, Pa.

Vacancies

No. 101—For a young man, graduated from a good school, and with good hospital training, who is particularly interested in clinical laboratory work and pathology, and who has also had some ground work in radiological work. Should be capable of heading up the entire laboratory department, including the clinical laboratory and the x-ray department. Preference for an unmarried Protestant. Location in the South.

No. 102—A young man who has finished his interneship and a residency is wanted to fill an appointment of Assistant in Medicine at a Clinic in the East. The work consists of general medical examinations and diagnosis. Special opportunity in cardiovascular disease and thyroid disease. The appointment would be made for one year at a time.

Appointments Desired

No. 1—Internist, M.D., F.A.C.P., 38 years of age, married, ten years private practice, desires association with older man or clinic where there are opportunities for advancement. Mainly interested in diseases of chest and stomach. Will go anywhere but prefers city in Southwest. Personal interview may be arranged.

No. 3—An Associate of the College desires an assistantship, associateship or partnership in Chicago; 40 years of age; M.D., Rush Medical College; wide experience in both teaching and practicing Pediatrics.

No. 4—An Associate of the College desires an assistantship or an association with some good clinic; willing to go anywhere, if there is a promising future; personal interview desirable, as well as period of probation to show ability; extensive training and experience in diseases of the heart and lungs and in insurance examinations; age, 36, married; M.D., Tulane University; postgraduate work in Internal Medicine at New York, Chicago, Philadelphia and Mayo Clinic; special examiner during World War in diseases of heart and lungs; since engaged in civil practice, doing only Internal Medicine, with important teaching and hospital appointments.

LIFE MEMBERSHIP

The By-Laws of the American College of Physicians provide specifically for an Endowment Fund, the chief part of which shall be made up of moneys received for Life Membership in the College. Quoting the By-Laws specifically:

> "It shall be the duty of the Board of Regents to provide a plan for securing an adequate endowment, the principal of which shall be held intact and invested in securities approved by the Board of Regents, while the income shall be available for carrying out the purposes of the organization. Such endowment fund shall consist of: (1) all moneys received for Life Membership in the College; (2) such moneys as may be set aside by the Board of Regents from time to time from the funds of the College, and (3) such moneys as may be donated directly to the fund."

The most important provision is that this Endowment Fund becomes a financial guarantee for the stability of the College, and also assures the accumulation of funds for special purposes. An illustration of one of the immediate results of the present fund has been the founding of a Fellowship in

Research to be known as the "John Phillips Memorial Fellowship." The details of the awarding of this prize or Fellowship will be published in the near future.

Many Fellows of the College have recommended that the organization adopt a plan for the examination and certification of hospitals, clinics, etc. Such a program would call for a large expenditure every year, and cannot well be financed without specific income other than from initiation fees and dues.

The initiation of sectional meetings at points remote from the annual meeting places, giving opportunity to Fellows and Associates of the College to receive additional postgraduate work, even though they are unable to attend the annual sessions, has been another project advanced by several. An adequate Endowment Fund would make many such projects possible.

In lieu of annual dues, a Master or Fellow may become a Life Member of the College upon the payment of $500.00 in cash, or $100.00 each year until $500.00 has been paid. In case a member desires to pay for life membership by paying $100.00 yearly for five years, his annual dues shall cease when he has paid three annual payments of $100.00 each. The original $100.00 fee paid at time of initiation is applied on this fund, thus making it really necessary for a Life Member to pay but $400.00. The following are already Life Members:

Dr. Lewellys F. Barker
Baltimore, Md.
Dr. Oscar Berghausen
Cincinnati, Ohio
Dr. Robert Bernhard
New Orleans, La.
Dr. Carl R. Comstock
Saratoga Springs, N. Y.
Dr. Ernest H. Falconer
San Francisco, Calif.
Dr. J. A. Lepak
St. Paul, Minn.
Dr. Charles F. Martin
Montreal, Que.
Dr. Nels C. Meling
Evanston, Ill.
Dr. Francis M. Pottenger
Monrovia, Calif.
Dr. Austen Fox Riggs
Stockbridge, Mass.
Dr. John G. Ryan
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Dr. Adolph Sachs
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Dr. William D. Sansum
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Dr. Frank Smithies
Chicago, Ill.
Dr. Alfred Stengel
Philadelphia, Pa.
Dr. Noxon Toomey
St. Louis, Mo.
Dr. M. L. Turner
Berwyn, Md.
Dr. A. H. Waterman
Chicago, Ill.
Dr. Bernard L. Wyatt
Tucson, Ariz.

NOMINATING COMMITTEE FOR 1931

In accordance with the provision of the Constitution, President Sydney R. Miller appointed the following Nominating Committee, during early March, to bring in nominations at the next Clinical Session for elective line Officers, Regents and Governors:

Dr. Alfred Stengel, Philadelphia, *Chairman*
Dr. James H. Means, Boston
Dr. James S. McLester, Birmingham
Dr. Ernest B. Bradley, Lexington
Dr. Egerton L. Crispin, Los Angeles

OBITUARY

Dr. J. Watson Campbell (Fellow), Halstead, Kansas, died January 27, 1930, of coronary thrombosis, aged 46.

Dr. Campbell received his A.B. degree from the Kansas University in 1909, and his medical degree from the Medical school of the same institution in 1914. From 1914 to 1920, he was Laboratory Assistant in the Kansas City General Hospital; from 1917 to 1924, Laboratory Director at the Swope Settlement (Kansas City); from 1920 to 1924, Laboratory Director of the Kansas City General Hospital; from 1921 to 1924, Laboratory Director of the Christian Church Hospital of Kansas City, and since 1924, he had been Chief of Medicine in the Halstead Hospital.

Dr. Campbell was a member of the Harvey County (Kansas) Medical Society, the Kansas State Medical Society, the Kansas City Academy of Medicine and a Fellow of the American Medical Association. He was elected a Fellow of the American College of Physicians on March 8, 1928, during the New Orleans Clinical Session. He was held in high esteem by the medical profession of his state.

Dr. George F. Roberts (Fellow), Salt Lake City, Utah; died, March 30, 1930, from acute hemorrhagic nephritis; aged 44 years. The cause of his death may have been superimposed upon an old chronic nephritis resulting from an accidental taking of bichloride while in the war in 1917.

Dr. Roberts was graduated from the University of Utah with a B.A. degree in 1910. He received his medical degree from Rush Medical College in 1912, had his internship in St. Mark's Hospital, Salt Lake City. He did postgraduate work at the Mayo Clinic in 1925 and in various New York City clinics during 1927. At the time of his death, Dr. Roberts was Visiting Physician to the St. Mark's Hospital in Salt Lake City.

He served as a First Lieutenant in the National Guard of Utah on the Mexican border in 1916, and as a Captain and Major in the World War from 1917 to 1919.

Dr. Roberts had the unique experience of being drowned in a lake while enroute to France. He was unconscious for several hours from this but made, apparently, a complete recovery.

He was a wonderfully fine man, as well as being a very competent internist; he will be greatly missed in his community.

—Furnished by G. G. Richards, M.D., F.A.C.P., Governor for Utah.

Dr. Wilfred Mason Barton (Fellow), Washington, D.C.; died, April 3, 1930, at the Mayo Clinic, Rochester, Minnesota, of peritonitis, following an operation.

Dr. Barton was born July 16, 1871, in Washington, D.C., educated at Central High School, from which he graduated in 1899, and later received the degree of M.D. at the Georgetown University Medical School in 1892. He also held the degree of Master of Arts. Dr. Barton pursued postgraduate courses for six months during 1909 at the Allgemeines Krankenhaus and three months among Paris hos-

pitals. He was Professor of Pharmacology and Therapeutics in the Medical Department of the Georgetown University from 1906-1916, and Associate Professor of Medicine, in the same institution, from 1916-1927. At the time of his death, he was Professor of Theory and Practice of Medicine at his alma mater, Attending Physician to the Georgetown University and Gallinger Hospitals, and Consultant to the Columbia Hospital for Women.

He was a member of the Medical Society of the District of Columbia, having been President in 1911; a Fellow of the American Medical Association; a member of the District of Columbia Clinical Society; a member of the Clinico-Pathological Society of the District of Columbia; a member of the Society of Nervous and Mental Diseases of the District of Columbia; and had been a Fellow of the American College of Physicians since 1923.

He was the author of "Thesaurus of Medical Words and Phrases" (1903); "Manual of Vital Function-Testing Methods" (1916); "Therapeutic Index" (1917); "Medicine" in Collier's Popular Science Library (1922); "Symptom Diagnosis" in the Appleton Series (1927); "The Road to Washington" (Historical—1919); and numerous other papers on miscellaneous subjects.

Dr. Barton was a member of the Board of Appeals of the District, served during the World War, and was formerly First Lieutenant in the Medical Reserve Corps of the Army. He is survived by his wife, Mary Quinn Barton, formerly of Boston, Mass.

—*Furnished through the courtesy of the Medical Society of the District of Columbia.*

New Books

PERNICIOUS ANAEMIA

By L. S. P. Davidson, B.A.(Camb.), M.D., F.R.C.P.E., Lecturer in Systematic and Clinical Medicine, University of Edinburgh, etc.; and George L. Gulland, C.M.G., LL.D., M.D., F.R.C.P.E., Professor Emeritus of Medicine and Clinical Medicine, University of Edinburgh. Appendix on Dietetic Treatment by Ruth Pybus, Sister Dietitian, Royal Infirmary, Edinburgh. Introduction by L. D. Thompson, M.D., Asst. Prof. of Clin. Med., Washington University School of Medicine. 407 pages, 6¼ x 9¾, 8 illustrations and 22 plates, of which 12 are colored. Price, cloth, $8.50. This new work fills a real need in medical literature. The authors have expressed with simplicity the essential features of symptomatology, diagnosis, and treatment of pernicious anaemia. Just published.

PHYSIOLOGY AND BIOCHEMISTRY IN MODERN MEDICINE

By J. J. R. Macleod, M.B., LL.D., D.Sc., F.R.S., Professor of Physiology in University of Aberdeen; and others. 6th revised edition. 1074 pages, 295 illustrations, 9 color plates. Cloth, $11.00. Few medical books published in recent years have achieved the popularity of this one. Physicians and surgeons have found it invaluable in their daily work. Completely revised and enlarged. The Jour. A. M. A. says "The book has great potential value because it presents adequately the knowledge of these sciences that the physician can use to deepen his grasp of the nature and meaning of the phenomena of disease."

SYMPTOMS OF VISCERAL DISEASE

By F. M. POTTENGER, A.M., M.D., LL.D., F.A.C.P., Medical Director of Pottenger Sanatorium, etc. 4th revised edition. 426 pages, with 87 illustrations and 10 full page color plates. Cloth, $7.50. This is a study of the vegetative nervous system in its relation to clinical medicine. Pottenger believes that the patient who has the disease should receive equal consideration to the disease which has the patient. Invaluable to surgeons.

DISEASES OF WOMEN

By H. S. CROSSEN, M.D., F.A.C.S., Professor of Clinical Gynecology, Washington University Medical School, and R. J. Crossen, M.D., Instructor in Clinical Gynecology and Obstetrics, Washington University Medical School, etc. 7th revised edition. 1009 pages, with 934 text illustrations and 2 color plates. Cloth, $11.50. A new edition of a Crossen book is a matter of some moment in medical publishing circles. The new seventh edition of "Diseases of Women" like those preceding it will prove invaluable to the physician and surgeon with problems to solve involving gynecological procedure.

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